A HAND-BOOK

OF

OCULAR THERAPEUTICS

BY

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THIRD EDITION, THOROUGHLY REVISED

ILLUSTRATED WITH 69 ENGRAVINGS

LEA & FEBIGER

PHILADELPHIA

TO

THE MEMORY OF MY FATHER

HAROLD GIFFORD

TO WHOSE KNOWLEDGE, JUDGMENT AND PAINSTAKING CARE

OF HIS PATIENTS

ANYTHING OF VALUE IN THIS BOOK IS DUE

PREFACE TO THE THIRD EDITION.

To anyone interested in therapeutics it must seem that the four years since the Second Edition of this book appeared have been the most exciting within the recollection of most of us. When looking up the subject of Vitamins recently, the author was horrified to find in his own book the following bald statement: "No ocular diseases are known to be associated with a deficiency of Vitamin B." This statement, true in 1937, has required 4 pages of type for its rectification in 1941. A complete re-writing of the Section on Vitamins has been rendered necessary by accessions to our knowledge, including the work of Carroll and Johnson on the effect of vitamin B_1 in toxic amblyopia and that of Johnson, Sydenstricker and others on corneal changes due to riboflavin deficiency.

In 1937 sulfanilamide and its derivatives were just being used in general infections, but no important reports on their use in diseases of the eye had been made. The great importance of this group of drugs has required a rather full discussion, in which rationale, dosage and special indications for the various drugs are considered.

Studies of the sympatho-mimetic and parasympatho-mimetic drugs which have immensely clarified our conception of their mechanism were in progress in 1937 but received no consideration in the Second Edition. The results of these studies with conclusions as to the synergistic and antagonistic effect of various drugs have been considered in this revision.

Some newer drugs, about which little or nothing was known in 1937, such as mecholyl, prostigmine and furfuryl trimethyl ammonium iodide are included in the discussion.

A number of advances in physical and irradiation therapy have been discussed, including the contact method of irradiation for retinocytoma and the use of beta-emanations in tuberculosis ol the anterior segment and vernal conjunctivitis. Some additional notes as to the use of buffer solutions and preservatives for ophthalmic solutions have been included. A few new illustrations have been added.

Discussion of some therapeutic agents which are out-of-date has been eliminated and that of other agents bas been condensed.

The bibliograpby concerning new therapeutic agents and procedures has been, so far as possible, brought up to date and completed with the idea that the book may serve to some extent as a reference work on modern therapeutic procedures. It is interesting to note how many of these later contributions have been made by Americans.

In addition to previous acknowledgments, the author takes pleasure in thanking Dr. Irving Puntenney and Miss Victoria Catalina for tbeir belp with the illustrations, and Miss Irene Carter and Miss Estelle Giza for their work with the manuscript.

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PREFACE TO THE FIRST EDITION.

My excuse for attempting a work of this kind is the absence in English of a recent concise book on therapeutics. In the larger works on this subject a profusion of information is to be found from which it is sometimes difficult to select the essentially valuable procedures from the purely traditional ones. Also a number of valuable modern procedures have come into use since any of these works were written.

Here no attempt will be made to trace the history of therapeutics and it is proposed to consider only such procedures as have proven themselves effective in my hands or in those of ophthalmologists whose opinion is considered of undoubted value. Chapter bibliographies will not attempt to cover the literature, but only to make available a few works which should be consulted for more detail than can be included here.

It has been impossible to avoid entirely a discussion of pathogenesis and diagnosis, but an attempt has been made to bring these in only where they definitely relate to treatment. Surgery will be discussed only in so far as concerns the indications for operation, except for certain minor procedures which may be considered as a part of office treatment.

It is a pleasure to acknowledge with thanks the help of Miss Dorothea Mazanec-Engelhardswall, Miss Madge Walsh and Miss Mary Dixon, in preparing the illustrations, and of my wife, Alice Gifford, with the proofs and index.

S. R. G.

Chicago, Illinois

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OCULAR THERAPEUTICS.

INTRODUCTION.

Any opinions which have ever been expressed on the subject of therapeutics are open to the objection that, in dealing with diseases, the defensive mechanism of the body offers variable factors whose importance cannot be estimated. The difficulty of estimating the value of therapeutic agents administered in an attempt to aid this mechanism is, therefore, obvious. This explains the remarkable variance in reports of different observers and often of observers whose clinical judgment is usually very reliable, as to the effect of various therapeutic agents. A chance series of cases with a fortunate outcome may convert an ophthalmologist of unquestioned standing into an enthusiastic advocate of a measure which has little to recommend it theoretically, and which in the hands of other men may later prove absolutely worthless. Thus it is necessary to greet the first reports on tbe use of any new agent with a certain amount of reserve. Agents of recognized value sbould not be abandoned in favor of new ones unless the evidence in favor of a change is convincing. The evidence of a small number of case reports alone is apt to be unsatisfactory, and one will be slow to take up the use of a new method unless there exists a certain foundation of theoretical and experimental reasons why the new method is likely to prove of advantage.

A position of therapeutic nihilism, or of unreasoning scepticism with regard to new agents and methods, is equally fallacious, as is the position of resting content witb time-honored methods, some of which have nothing but the sanction of years to justify their continued use. In ophthalmology, especially, there are certain objective signs, such as

the size of the pupil, the intraocular tension, the presence of congestion, hypopyon and other measurable conditions, which should place us at an advantage in judging the effect of therapeutic agents. Certainly an important duty of the scientific ophthalmologist, especially of the one with a large amount of clinical material at his disposal, is to give a thorough trial to agents and procedures which, for theoretical or other reasons, seem to fill a gap in our therapeutic equipment. Such trials should, of course, be conducted with every possible precaution of careful observation and control, and their results, whether favorable or unfavorable, should be reported for the benefit of men with less material at their disposal.

In using any therapeutic agent, new or old, a factor no less important than the knowledge of how to use the agent, is that of careful observation of each case. It must be determined as soon as possible whether or not the desired effect is being produced, so that, if it is not, other methods may be applied without loss of valuable time. Naturally such observation is especially important where newer agents are being employed.

A great many statements found in these pages will undoubtedly be considered overenthusiastic or radical, while others will be considered unduly sceptical in the face of favorable evidence. It can only be said that an attempt has been made to form an honest judgment on disputed questions, and that failure to express such opinions would, in the author's belief, deprive the book of any practical value it might conceivably possess.

CHAPTER I.

EQUIPMENT.

In order that the ophthalmologist's therapeutic resources may be used to the best advantage, a certain minimum of physical equipment is necessary. Many offices well equipped for refraction and diagnosis provide meagre facilities for cases requiring treatment, such cases being sent to the hospital wherever possible. Patients are quick to realize when work is being done under unfavorable conditions and appreciate a little effort to provide for treating simple conditions in the office.

It is undoubtedly of great advantage to have a room set aside for treatment and minor operative procedures. This room may be arranged to make use of the best daylight available and should be large enough to contain a small operating table or adjustable chair, instrument cabinet, sterilizer and other equipment. Minor operations, such as curettage of chalazia, destruction of lashes, and probing of the naso-lacrimal duct may be carried out quite efficiently in the office if such an arrangement is available. The services of a nurse or trained office assistant are valuable but not absolutely essential in such office procedures. Where space for a separate room is not available, a portion of the room used for refraction may be made reasonably convenient.

A simple plan for a small one-room office is shown in Fig. 1. The patient's chair should face a window, as daylight is essential in examining the conjunctiva and cornea, especially after staining with fluorescein. A bright source of focal illumination is also necessary for detecting small foreign bodies or erosions. The bull's eye lamp, fixed on the wall so as to focus on the average patient's face, is convenient, and even better, where one has an assistant, is the

Shahan operating light or the Hammer lamp. The Shields operating lamp gives an especially bright light and may be focussed accurately, while its stand avoids the necessity of

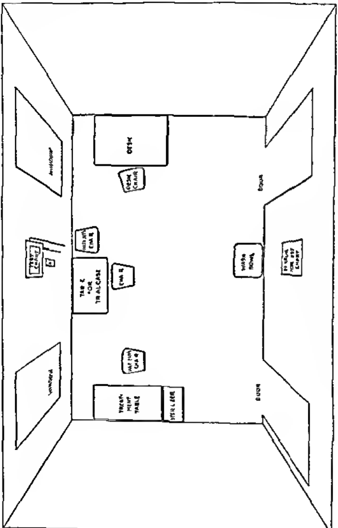

Fig. 1.—Plan of room for treatments and trial case tests.

an assistant to hold the light. (See Fig. 2.) No ophthalmologist's office should be without some type of binocular loupe. Many convenient tables are available, with permanent places for the solutions in common use, and shelves for supplies. Solutions should be kept in bottles with fitted ground-glass droppers so that they will remain clean and unmixed with other solutions. If each bottle is always kept in the same place, besides being plainly labelled, mistakes in their use are easily avoided. *Solutions* which are to be kept *should be protected against the growth of fungi in some way*, and a convenient method is the addition of 40 grains of boracic acid crystals to the ounce of each solution, the excess of crystals being left in the bottle. The solutions used by each ophthalmologist will vary, but the following list will provide for most office treatments: 1 per cent cocaine hydrochloride, 10 per cent cocaine hydrochloride, 1 per cent butyn sulphate, 1 per cent atropine sulphate, 0.2 per cent escrine sulphate, 2 per cent homatropine hydrobromide, 2 per cent silver nitrate, 0.2 per cent zinc chloride, 2 per cent zinc chloride, 1 to 1000 adrenalin, 5 per cent dionin in 1 to 5000 mercuric cyanide, 1 per cent fluorescein. To all of these except silver nitrate and adrenalin, boracic acid crystals may be added. A large bottle should be kept filled with boracic acid solution or normal saline for the irrigator and small glass-stoppered

Fig. 2.—Shields' lamp.

bottles for trichloracetic acid, iodine solution and for optochin and mercurochrome crystals. Small glass dishes such as those used by dentists for mixing cement are very convenient for local applications to the cornea, as a few grains of optochin or mercurochrome can be placed in such a dish so that the whole bottle is not moistened or contaminated by the applicator. A supply of gauze cut in small squares and of small

FIG 3.—Small dental burs for removing rust rings from the cornea.

sponges may be sterilized dry and kept in glass jars. Small sterile tooth-pick applicators covered with a very small amount of cotton are useful for sponging or applying local anesthetics directly to the conjunctiva or lacrimal apparatus.

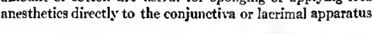

FIG 4.—Corneal applicator.

Unless there is room for a small operating table, the chair for treatments should be adjustable so that the patient may be brought into a reclining position for taking the tension or for minor operations.

The instruments for an office need not be very numerous if they are well chosen. The following list contains a few things which one cannot do without.

Scissors: 2 sharp, fine-pointed and curved; 1 bandage scissors.

Knives: 1 scalpel, 2 or more cataract knives that have been ground down, but are very sharp.
Forceps: 1 fixation, 1 thread forceps, 1 fine-toothed forceps, 1 needle-holder, 2 pairs cilia forceps, 1 trachoma forceps.
Fine needles and black silk.
Spuds: several sizes, including 1 fine-grooved spud.
1 set of fine dental burs for removing rust rings from cornea.
1 chalazion clamp.
2 small sharp spoons.
1 tuberculin syringe.
1 fine lacrimal dilator.
Lacrimal probes: 1 set Bowman's probes, Nos. 1 to 14, 1 Weber probe, 1 grooved probe.
1 fine probe-pointed lacrimal knife.
1 set gold lacrimal needles for Luer syringe.
2 eye specula, 1 of baby size.
2 lid hooks.
3 corneal applicators.
3 small curved pus-basins for irrigations.
Copper-sulphate crystals and holder.
3 1½-cc. Luer syringes.
1 tonometer.

The instruments, especially the scissors and forceps, should be of the delicate size and construction suitable to eye-work. Lacrimal dilators and probe-pointed knives are often furnished with such large tips as to make them practically useless but small ones can be obtained and should be insisted upon. Naturally they must be kept in the best possible condition by constant examination, especially knives, scissors and the teeth of forceps. (Fig. 5.)

A simple apparatus for destroying lashes and small growths of the lids is considered necessary by most ophthalmologists. A switchboard and converter to produce high frequency current for electrolysis may be installed on the wall of the

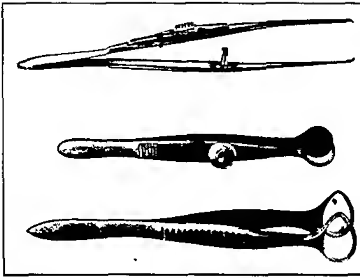
A
B
C

Fig 5 —*A*, fixation forceps (H. Gifford); *B*, chalazion clamp, *C*, trachoma forceps (H. Gifford).

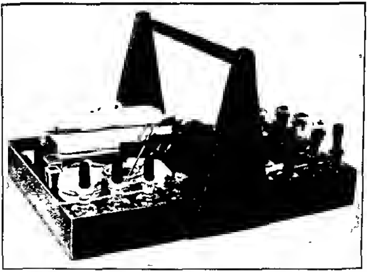

Fig 6 —Tray for ocular dressings and treatments in hospital.

treatment-room or the small unit of Walker utilizing a large storage battery with Walker's very fine needles may be preferred. A surgical diathermy unit may be employed for the same purpose. (See p. 162.)

Every ophthalmologist will have individual preferences which will lead him to modify this list, and the only object of this discussion is to emphasize the importance of having suitable equipment in the office so that one need not shrink from carrying out treatment and minor operations on patients who cannot be hospitalized. An equipment similar to the above should be on hand at the hospital where one's eye patients are sent. The tendency in modern hospitals is to have rooms set aside for special types of work and a room such as described above can be arranged in any hospital at very small expense. Fig. 6 shows a convenient tray for treatment and dressings in rooms or wards.

A detail which may not be considered so necessary, but which the author considers important, is the provision of material for making simple bacteriological examinations in the office. All that is necessary for this is a Bunsen burner, a sharp platinum spatula for making epithelial scrapings, some glass slides, the materials for a Gram stain and a microscope. Where one is in the same building with a good clinical laboratory the staining and examination of slides can be made there, but if a technician must be called in for smears the inevitable tendency is to neglect this examination in a number of cases where the information obtained would be valuable from a therapeutic standpoint.

CHAPTER II.

ANESTHETICS, NARCOTICS AND HYPNOTICS.

GOOD anesthesia is an essential to efficient treatment or operations in the region of the eye. The ophthalmologist is fortunate in being able to carry out most procedures under local anesthesia. The first medical use of *local anesthesia* was made by Koller's introduction of cocaine in 1882, for ophthalmic cases. The only conditions under which general anesthesia is required are in the case of small children, very nervous or hysterical patients, for a few extensive operations, such as evisceration of the orbit, plastic restoration of the conjunctival sac, or operation for acute glaucoma where the tension cannot be reduced before operation. Where local anesthesia is carefully planned and carried out with every effort to retain the patient's confidence, children as young as ten or twelve years of age will sometimes permit short operations under local anesthesia.

The method of local anesthesia most commonly used is that of instillation. Most of the local anesthetics, cocaine, pontocaine, novocaine, nupercaine, butyn and others, are absorbed readily by the conjunctiva, cornea and lacrimal passages, allowing good anesthesia for surface procedures by instillation alone. Novocaine is not so well absorbed and is usually reserved for infiltration.

Cocaine.—*Cocaine has the disadvantage of causing dilatation of the pupil and drying of the corneal epithelium*, hence certain precautions must be observed in its use. It must not be used where glaucoma is suspected unless the case is observed afterwards and a miotic is given to counteract its mydriatic effect It must never be used in acute glaucoma. When it is used the patient must keep the eyes closed except during the actual time of treatment or operation, and a dressing must be worn for several hours after the treatment is completed. *It has an advantage over all of its substitutes, besides*

its rapid and complete effect, in that it causes depletion of the vessels, which is of advantage in treating conjunctival conditions, such as trachoma, and that it aids in the absorption of certain other drugs, especially atropine. For minor procedures, such as applications to the conjunctiva or removal of foreign bodies, a 2 per cent solution is sufficient, 2 drops being instilled at two-minute intervals. For more extensive procedures, such as enlarging the tear-points, probing the lacrimal duct or excising small papillomata, 4 or 10 per cent solution is necessary. These stronger solutions are best applied directly to the desired spot on a small tooth-pick applicator, preceded by a drop of 2 per cent cocaine, as the 10 per cent solution itself is somewhat painful when applied to the unanesthetized conjunctiva. Then two or three applications of the 10 per cent solution are made at two-minute intervals, after which the tear-point may be dilated or a pterygium may be removed without pain. For intraocular operations 2 to 5 per cent cocaine is usually employed. Many operators perform cataract extraction with instillation only, but there is usually some pain when the iris is excised, and perfect anesthesia can only be assured by the injection of 1 or 2 minims of cocaine (2 or 4 per cent) or one of its substitutes over the site of fixation and near the upper limbus. In order that the injection itself may be painless, this should be preceded by instillation of 2 per cent cocaine once and 5 per cent cocaine three times at two-minute intervals. After injection four minutes should be allowed before the incision is made. Such perfect anesthesia is, of course, very important in any intraocular operation, to prevent the patient from pressing the lids together, which may have disastrous results. For such an involuntary reflex the surgeon must hold himself responsible as the patient cannot avoid it if pain is felt. Hence every care to prevent it is not too much for the surgeon who desires the highest possible percentage of successful results. *Other means of preventing blepharospasm will be discussed later, but the first requirement is perfect anesthesia.*

Anesthesia of the lacrimal passages will be discussed in the chapter dealing with their treatment. Here it may be said that by applications of cocaine to the tear-points they may be dilated painlessly, after which cocaine solution may be injected through the canaliculi into the lacrimal sac and often through the nasolacrimal duct into the nose. After one or two such injections probing may be carried out with a minimum of pain, and should never be attempted without every effort at good anesthesia.

The use of cocaine by instillation or injection of 1 to 3 minims of 4 per cent solution subconjunctivally involves practically no danger of general toxic effect. Though the toxic dose of cocaine varies with different patients, it may be said for practical purposes to be always above this amount, so that the rule now applied in general surgery, that safer substitutes for cocaine shall always be used for injection, need not be applied to ophthalmology where the above dosage is strictly observed. As to the toxic effects of cocaine upon the eye itself, Poos and other authors have pointed out a damage to the vessels involving greater danger of hemorrhage after much cocaine has been used, while others are cautious because of possible delay in the healing of tissues exposed to strong solutions of cocaine. These considerations must be borne in mind when dealing with such a toxic product, but the results of many ophthalmologists' experience with a technique resembling the above has made it evident that these dangers are less than those involved in insufficient anesthesia or in general anesthesia, where this can be avoided. It need hardly be said that the amount of cocaine used must be kept to the minimum necessary for absolutely satisfactory anesthesia, and for this solutions stronger than 5 per cent are unnecessary.

While cocaine remains our most widely used anesthetic for local application, *a number of substitutes possess definite advantages over cocaine in certain conditions.* As stated before, cocaine causes mydriasis by active stimulation of

the dilator iridis. Holocaine and butyn are without this effect, while having an anesthetic effect practically as active. *Holocaine, pontocaine and butyn produce their effect much more rapidly than cocaine, and have no drying effect on the corneal epithelium*, so are especially useful for removing foreign bodies and taking the intraocular tension, since a dressing afterwards may usually be dispensed with. Neither of these drugs constricts the vessels; in fact, both are slightly irritating and cause congestion, so are unsuitable for most intraocular operations, or for use in treating corneal ulcers or other conditions in which the eye is already congested, though this effect may be counteracted by adrenalin. Holocaine is used in 1 per cent solution for instillation, and enough dilute acetic acid must be added to give a faintly acid reaction to litmus, otherwise the solution is unstable. It is slightly more irritating than 2 per cent butyn, but both act with almost equal rapidity, so that after 2 drops are given, one minute apart, the tension may usually be taken, or a foreign body removed. It is probably safest to use one of these drugs for removing foreign bodies, since the damage to the corneal epithelium from cocaine combined with that caused by the spud may cause a troublesome erosion, while this damage is certainly minimized with holocaine or butyn. *Neither drug is adapted to injection*, since holocaine decomposes when sterilized in glass, so must be sterilized in porcelain containers, and is also irritating to the tissues, while *butyn is exceedingly toxic for certain persons with an idiosyncrasy*, so that the Committee on Anesthetics of the American Medical Association advises against its use by injection. Lemoine and a few others have reported on idiosyncrasies to butyn when used by instillation, a severe conjunctivitis and dermatitis having been caused in several cases.

The author has seen a number of annoying reactions following practically all the substitutes for cocaine in common use. These are more common in persons who have been given a weak anesthetic to use for relief of conjunctival or

corneal irritation but some have occurred after one instillation in persons with a marked idiosyncrasy. Some especially severe local reactions have occurred with pontocaine, a case reported to the author by Dr. H. W. O'Neill of Santa Ana, California, having lost all the corneal epithelium following 2 drops of 1 per cent pontocaine. One such reaction in the author's practice was especially confusing as it occurred in a patient who was using eserine. The severe conjunctivitis was attributed to the latter drug until it was noted that it

FIG. 7 —Dermatitis and conjunctivitis due to butyn.

always became worse, even when eserine was stopped, after taking the tension with butyn. (See Fig. 7.) Such occasional reactions form no contraindication to the use of such useful anesthetics as butyn and pontocaine but must be watched for and when once such a reaction has occurred special precautions must be taken to prevent use of the same drug by the ophthalmologist or an assistant. Some other anesthetic must be employed in such patients who must be treated or examined repeatedly. The use of 0.5 to 1 per cent cocaine in such cases has never caused local reactions in the

author's experience and must sometimes be employed, with precautions against drying of the cornea.

While the 2 per cent solution of butyn commonly used is distinctly painful at the first drop, a 1 per cent solution is much less so, and has proven perfectly effective in taking tension and removing foreign bodies. Hence it may well replace the 2 per cent solution for these purposes.

In *operations for acute glaucoma*, where one fears any additional dilatation of the pupil, *anesthesia is best secured by instillation of holocaine or butyn, followed by a deep orbital injection of novocaine.* (See below.) Holocaine, besides its use as an anesthetic for treatments, is of use in certain chronic epithelial dystrophies with multiple small erosions. A 1 per cent ointment or 0.5 per cent solution is used by the patient several times a day.

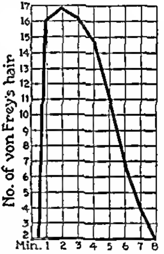

Fig. 8 —Duration and depth of anesthesia obtained with 2 per cent cocaine. (From Bellows)

Either this or a 0.5 per cent solution of butyn may be used freely after burns of the conjunctiva, pterygium operations, foreign-body removal, or after other superficial disturbances likely to cause pain. Where patients complain of pain caused by other necessary drops, such a solution may be used by the patient before these drops are given.

A number of other substitutes for cocaine for use by instillation have been proposed, with various advantages claimed to justify their use. Marx and associates have compared some of these, including novocaine, novocaine borate (borocaine), psicaine, eucaine, tutocaine, diocaine and eucupin, with cocaine, and found that *none of these drugs equalled cocaine*

in the principal requirements of a local anesthetic. Most caused congestion, which would contraindicate their use in operations, and some, such as eucupin, were too painful on the first instillation. Tutocaine, which is much used in Europe, produced congestion and was only one-eighth as effective as cocaine. A quinine derivative, nupercaine, has recently been advocated in general surgery on account of its pro-

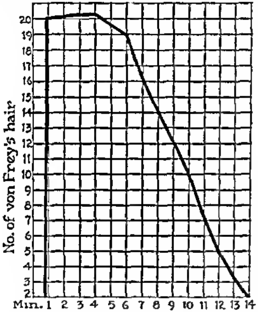

FIG 9 —Duration and depth of anesthesia obtained with 0 5 per cent pontocaine. (From Bellows)

longed anesthetic effect, and the consequent freedom from after-pains following its use for operations. Dillon and Greer have found that instillation of a 1 to 1000 to 1 to 500 solution is sufficient to allow recording the tension or removing a foreign body and that operations such as that for pterygium could be done with less after-pain than when cocaine was used. Anesthesia is slow with nupercaine, however, and some operations require injection of the drug for effective

anesthesia. When this is necessary the same small amount must be used as with cocaine, as the drug is equally toxic. If further experience bears out the apparent freedom from after-pain after its use, it may be advisable to employ nupercaine in combination with a more rapidly acting drug, such as novocaine, for certain intraocular operations.

Hoffman has recently studied most carefully some new substitutes for cocaine; diocaine, larocain and pontocaine, compared with older ones, testing corneal sensitivity with von Frey's hairs. *Only* **pontocaine,** *a derivative of novocaine, in 2 per cent solution, exceeded 4 per cent cocaine in the depth and duration of anesthesia secured.* Its greatest advantage over the other substitutes tested was in the regularity with which its effect was obtained in persons of varying sensitivity. Holocaine, for example, produced the deepest anesthesia of any drug in some persons but failed in others. Pontocaine had no effect on the pupil, but caused moderate conjunctival congestion. Wilmer and Paton have used pontocaine in 500 cases. They found that satisfactory anesthesia for minor procedures was secured by instillation of 0.5 per cent solution and evidently performed intraocular operations also after such instillations alone. They call attention to the fact that *the drug is ten times as toxic as novocaine but effective in much lower concentrations,* being used in general surgery by injection of 1 to 1000 solution.

A recent comparison of anesthetics used for instillation by Bellows offers evidence in favor of pontocaine. By combining the duration of anesthesia with its depth as measured by the von Frey's hair tolerated without pain, the anesthetic index of each drug was found. The index of 2 per cent cocaine being taken as unity, that of the other drugs tested was as follows:

Metycaine 2 per cent	0 45
Butyn 1 per cent	1 10
Holocaine (phenacaine) 1 per cent	0 81
Nupercaine 1 to 500	1 74
Pontocaine 0 5 per cent	2 33

See Figs 8, 9 and 10.

The effect of pontocaine was prompt, deep and prolonged. That of nupercaine 1 to 500 was much slower in onset but more prolonged than that of the other drugs tested.

The method of instilling anesthetics to produce the maximal effect will depend upon the type of treatment which is to be given. For an application to the conjunctiva of the lids, both lids must be everted, so that the drug will come into contact with as much conjunctiva as possible before it becomes diluted by the tears or escapes from the eye. For

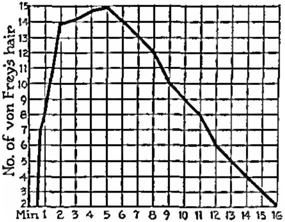

FIG. 10—Duration and depth of anesthesia obtained with nupercaine 1 to 500. (From Bellows)

removal of foreign bodies from the cornea or for tonometry it is best to have the patient in the horizontal position when the solution is dropped directly on the cornea while the lids are held apart for a second to retain it in the sac. If the patient is seated the upper lid should be held open and the solution dropped just on its border, so that it runs into the upper fold and over the cornea. If instilled in the lower cul-de-sac, the winking reflex may promptly eject the solution, while the cornea is turned up and receives no effect from the anesthetic.

Novocaine (procaine) *is the drug most suitable for injection where more than 2 or 3 minims must be employed.* It is absorbed very slightly from mucous membranes, so that its effect on instillation is unsatisfactory. It is only one-sixth to one-tenth as toxic as cocaine, 100 cc. of a 1 per cent solution being considered a maximal injection in general surgery. Its effect occurs less promptly than that of cocaine, so that at least five minutes must be allowed after injection before the operation is commenced. While 0.5 or 1 per cent solutions are considered of sufficient strength for use in general surgery, for operations on the lids, muscles or globe, such solutions do not give satisfactory anesthesia. A 2 per cent solution is most commonly employed, and this is advised by O'Brien and most authors who discuss local anesthesia. Bulson states that a 2 to 4 per cent solution may be used. *The author has found 2 per cent novocaine often unsatisfactory and would advise a 4 per cent solution for most procedures, the total amount of which should seldom exceed 2 cc.,* as Bulson suggests. When using the small amounts necessary for ophthalmic operations, seldom more than 1 or 2 cc., the danger of toxic symptoms with this solution is practically *nil,* and there is no reason why anesthesia should not be as complete as is safely possible. In large plastic operations, such as restoration of the orbit, a 2 per cent solution may be used, where general anesthesia is not preferred. The addition of 4 drops of 1 to 1000 adrenalin to the total amount of solution is usually advisable in any operation under novocaine, as it lessens hemorrhage and limits the absorption of the drug. More adrenalin than this may itself cause unpleasant symptoms. Novocaine is conveniently obtained in prepared sterile ampoules, which usually contain epinephrin.

In infiltration anesthesia a few drops should be injected just beneath the skin, and the remainder of the solution injected very slowly as the needle is advanced. *The whole area involved must be infiltrated thoroughly.* It requires a

surprising amount of pressure to infiltrate the extreme lid border, as is necessary for the trichiasis operations, but enough should be used to blanch the region completely. In operating upon chalazia it is important to surround the chalazion entirely with infiltration, the needle being passed finally beneath the chalazion, so that a few drops may be injected on its conjunctival side.

A. Fuchs has recently described a method of infiltrating for the chalazion operation which the author has since found extremely convenient. Injection of ½ cc. of 4 per cent novocaine is made *subconjunctivally in the retrotarsal fold at a point corresponding to the chalazion.* This blocks the nerves supplying it effectively, except where the chalazion is near the nasal end of the lower lid which is supplied by the first branch of the fifth nerve. This requires a small injection under the skin in addition to the retrotarsal injection. The subconjunctival injection has the advantage that previous instillation of butyn makes it absolutely painless and also that no externally visible hematoma from the needle puncture occurs as is often the case following subcutaneous injection.

In lid operations or expression of the folds for trachoma infiltration is usually perfectly satisfactory. The same is usually true of operations for removal or destruction of the lacrimal sac, providing injection is made directly into the lacrimal fossa close to the bone and near the opening of the naso-lacrimal duct. Complete anesthesia for probing is not obtained in this way, but if this is combined with injection of 10 per cent cocaine through the canaliculus into the sac, the pain is usually slight. O'Brien prefers nerve blocking for operations on the sac, and describes the technique of injecting the supraorbital, infraorbital and supratrochlear trunks for this purpose.

For muscle operations, especially tucking, complete anesthesia is hard to obtain, but it may be made almost complete in all cases and complete in a fair number by proper tech-

nique. Instillations of cocaine should be made as for a cataract operation. Then 2 minims of 2 per cent cocaine are injected subconjunctivally over the muscle to be operated upon. After one minute this muscle is grasped with fixation forceps, and *a needle, 2 cm. long, is inserted under the muscle and as far back as possible into the muscle cone, where 1 cc. of 4 per cent novocaine is injected.* It is absolutely essential that this injection be under the muscle, as otherwise pain will be felt when traction is made on it.

When more than one muscle is involved in the operation, retrobulbar injection is exceedingly useful as it avoids the edema which follows infiltration of the muscles and conjunctiva.

In enucleation or evisceration of the eye, or other operations on the orbit, and in operations for acute glaucoma, *retrobulbar anesthesia is essential.* The same method is employed by many surgeons in cataract operations, but when novocaine-adrenalin is used a marked hypotony of the globe results which, while it helps to prevent vitreous loss in the intracapsular operation, makes the expression of the lens by the capsulotomy method exceedingly difficult.

A recent article by Atkinson discusses all types of local anesthesia and another by Apin deals with the particulars of orbital anesthesia alone. *Injection into the muscle-cone* anesthetizes the ciliary ganglion, the long and short ciliary nerves and the naso-ciliary nerve. It also paralyzes all the nerves to the extraocular muscles except that to the superior oblique. *It thus produces insensitivity of the entire globe and its contents and of the extraocular muscles.* It affords satisfactory anesthesia for intraocular operations and for removal of the globe or its contents. *For complete anesthesia of the entire orbital contents, as in evisceration of the orbit, it is also necessary to inject the frontal, lacrimal and infraorbital nerves.*

Retrobulbar injection may be made either through the conjunctival sac (see Fig. 11) or through the skin. (Fig. 12.) The needle should be small (No. 2) so as to lessen the chance

of injuring blood-vessels, and 3.5 cm. long. With a needle of this length there is no danger of injuring the optic nerve if proper technique is followed. When injecting through

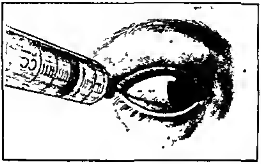

Fig. 11.—Technique of retrobulbar injection for removal of the eye (conjunctival route).

Fig 12.—Technique of retrobulbar injection for removal of the eye (external route) (from Atkinson).

the skin a small intradermal wheal is first made a short distance below the lower temporal margin of the orbit. Following this the needle is introduced slowly upward and inward,

passing just over the inferior orbital margin and being directed toward the apex of the orbit. A little solution is injected as the needle is introduced and if the patient is asked to look upward and to the opposite side the orbital fascia is put on the stretch, so that the needle passes easily and painlessly between the external and inferior recti. At a depth of 3.5 cm., the contents of the syringe are injected, usually 1.5 cc. of 4 per cent novocaine, to which 4 minims of 1 to 1000 epinephrine has been added. *If the needle is introduced slowly, hemorrhage into the orbit very rarely occurs*, while a rapid thrust is apt to injure a vessel, which may necessitate postponement of the operation.

Most intraocular operations should be performed as soon as the injection is finished before marked hypotony results from the injection. In cases of acute glaucoma it is often best to wait for this effect. *For enucleation it is best to wait five to ten minutes before operating.* There are few enucleations which cannot be performed painlessly with this technique, although certain patients will prefer general anesthesia to avoid a certain psychic trauma attendant upon enucleation of an eye, especially if it possesses vision.

An important adjuvant to local anesthesia in intraocular operations, and especially in the cataract operation, *is paralysis of the orbicularis muscle by the injection of novocaine to prevent pressure of the lids on the globe.* This was first described by van Lint as ocular akinesia, and has become a part of the routine preparation for the cataract operation with many ophthalmologists. While in most cases the danger of "squeezing" may be prevented by perfect anesthesia, there is no way to pick out the occasional patient who will "squeeze" even when no pain is felt. When vitreous loss occurs even the normal pressure of the lids may have serious results, and here previous akinesia is exceedingly valuable. *In order not to be taken by surprise under these circumstances, it is certainly the safest procedure to employ akinesia before every cataract operation.* It is equally impor-

tant after penetrating wounds, when a sliding conjunctival flap must be prepared, and where the wound is large, it is best to inject the orbicularis before the local anesthesia is begun. In operations for glaucoma, especially if blepharospasm is present, akinesia may also be valuable.

Van Lint's exact technique is as follows: 4 cc. of 2 per cent novocaine with 2 drops of adrenalin are injected, using

FIG 13.—Showing site of injection for akinesia according to van Lint.

a needle 3 cm. long. Puncture is made at the intersection of a horizontal line from the lowest part of the orbital border with a vertical line from the most external part of the orbital border. (Fig. 13.) Injection is made as far as the inner third of the lower lid, the needle being kept in contact with the periosteum at the orbital margin. If this precaution to inject deeply is not maintained akinesia will be incomplete and the lids themselves will be swollen with the injected fluid. One-half the solution is injected along this lower line, and then, without withdrawing the needle, it is

pointed upward along the outer border of the orbit, which is similarly injected. A second puncture must be made along the frontal prominence, from which the last part of the injection is made downward to join the previous injection. The upper border of the orbit in its outer two-thirds is injected from the second puncture. A wait of ten minutes is necessary before operating, when it should be impossible for the patient to close the eyes tightly. To avoid the use of such a large amount of fluid 1.5 cc. of 4 per cent novocaine may be injected in exactly the same way with equally good results, provided it is distributed very carefully along the same lines, and the effect of this injection is slightly more rapid, being usually fairly complete in five minutes.

To avoid the edema of the lids (which is not noticeable with 4 per cent novocaine) *O'Brien advocated injection of the facial trunk as it crosses the mandibular articulation.* The needle is entered just anterior to the tragus, below the posterior part of the zygomatic process, and is inserted about 1 cm. until it rests upon the condyloid process of the mandible; 2 cc. of 2 per cent novocaine are then injected as the needle is withdrawn. Paralysis begins in thirty to sixty seconds, and is complete in three to five minutes. In the author's experience this method has usually been satisfactory, but in an occasional case the nerve is missed and no akinesia is secured, while with van Lint's method some effect on the muscle is always secured, even if this is not in all cases a complete paralysis. (Fig. 14.)

In certain operations the induction of local anesthesia and subsequent procedures are much simplified by the preliminary use of narcotics. *These are especially necessary before muscle operations and enucleation or evisceration,* where slight pain may be felt or where traction on the muscles may cause nausea. In these operations the use of morphine sulphate, $\frac{1}{6}$ to $\frac{1}{4}$ grain, combined with atropine sulphate, $\frac{1}{120}$ grain, is usually satisfactory, the amount being decreased for children according to age. The use of scopolamine, $\frac{1}{100}$ to

$\frac{1}{200}$ grain, instead of atropine, produces ideal operating conditions in most persons. An occasional patient, however, reacts to scopolamine with a noisy and troublesome delirium, so that it is not advised as a routine procedure. In intra-ocular operations, especially the cataract operation, vomiting is to be avoided by all possible means, and since in many persons morphine causes vomiting, most operators omit morphine before these operations. One-half grain codeine

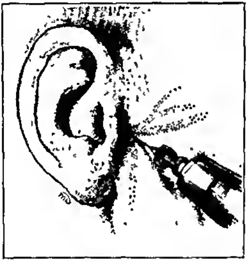

FIG. 14.—Site of injection for akinesia, according to O'Brien.

sulphate and 5 grains of phenacetine, given by mouth, however, one-half hour before operating, seldom causes vomiting and greatly lessens the after-pain. It may be repeated an hour after operating if pain is felt. A useful recent substitute for morphine is dilaudid, an opium derivative, of which $\frac{1}{32}$ grain may be injected and repeated postoperatively if necessary.

The *use of the hypnotics is preferred by some operators to the narcotics*, as by their means the patient is freed from anxiety during the operation, and goes to sleep when it is

over. Axenfeld gave 3 to 4½ grains of phenobarbital (luminal) to adults before operation, especially for acute glaucoma. O'Brien has used the large dose of 6 grains before all operations, apparently without ill-effects. Meyer gives the following schedule of preoperative doses for phenobarbital, as used in the Freiburg Clinic. In infants, aged four months, ⅓ grain; one year, ¾ grain; two years, $\frac{9}{10}$ grain; five years, 1⅓ grains; six years, 1½ grains; twelve years, 2½ grains; adults, 3 grains. He points out the advantages of phenobarbital for examination and roentgen-ray treatment of infants, and as a preliminary to operations under local anesthesia.

The author has found Meyer's schedule of the age-dosage useful, but is certain that *the dosage could be somewhat increased with better effect and with safety.* No ill-effects were ever seen from Meyer's dosage, but it produced little apparent effect in some small children. At a large children's hospital in Chicago, 1 grain of phenobarbital has often been given to children less than a month old as a substitute for anesthesia, without any bad results. A schedule of dosage for phenobarbital, slightly larger than Meyer's, which may be further increased by repeating one-half of the given dose an hour later in certain cases, follows:

From birth to four months, ½ grain;
Four months to one year, ¾ grain;
One to three years, 1 grain;
Three to six years, 1½ grains;
Six to twelve years, 2 to 2½ grains;
Adults, 3 to 4 grains.

Certainly a large number of infants who are now given a general anesthetic for fundus examination and investigation of the lacrimal passages could be spared this by some such preliminary treatment. An especially important indication for this seems to be in muscle operations, where results under local anesthesia are so much more accurate, since the previous *use of a hypnotic permits local anesthesia in children, aged* twelve to fourteen years of age, who would otherwise be

considered suitable only for general anesthesia. Where general anesthesia is necessary in children the use of these hypnotics in the same way greatly facilitates the induction of anesthesia and lessens the amount of anesthetic required. A number of modifications of barbital other than phenobarbital have come into recent use for which certain advantages are claimed, chiefly freedom from depressing effect and headache. Some of these, with the dosage which corresponds approximately to 1½ grains of phenobarbital or 7½ grains of barbital, are as follows:

Pentobarbital-sodium (nembutal) 1½ grains;

Sodium amytal, 3 grains; ipral calcium 3 grains; dial, 3 grains; neonal, 3 grains; ortal-sodium, 3 grains; seconal, 1½ grains.

A number of authors have recently advocated **rectal narcosis**, either alone or with the aid of local anesthesia. The drug usually employed is tribromethyl alcohol, the trade name for which is "avertin." By its means all degrees of anesthesia may be secured, from a mild analgesia, in which orders are obeyed, to complete anesthesia, lasting one to one and a half hours. This is followed by natural sleep, and no memory of the operative procedure is retained. A careful technique must be carried out in preparing and giving the drug, details of which will be found in the articles of Wessely, Wilmer, Morgan and Lees, and Davis.

The fact that avertin markedly reduces intraocular tension, as shown by Davis, may be of advantage in operations for acute glaucoma. Certain dangers are inherent in any method of rectal anesthesia, but with care in the hands of expert anesthetists these are little if at all greater than those of inhalation anesthesia. In a limited experience the author has found that the chief objection to avertin is its failure to produce satisfactory anesthesia in certain cases. This is especially common in children and most anesthetists prefer to limit its use to adults and adolescents. Use of preliminary

narcotics is essential to satisfactory effect and a small amount of local anesthesia is often necessary during the operation. Vomiting does occur after avertin in a number of cases, and hence its routine use in cataract surgery is hardly to be advised. In operations on the extraocular muscles, however, it presents certain advantages, including absence of chemosis due to local injections and of the discomfort felt by some patients in spite of careful local anesthesia.

Intravenous Anesthesia.—The use of various hypnotics by vein in dosage sufficient to produce anesthesia has been advocated for certain procedures by a number of ophthalmologists. The advantage of the method is that complete anesthesia may be secured, with almost immediate recovery and absence of vomiting or effects on the respiratory tract. Its use demands, as a rule, the services of a *physician in charge of anesthesia* who is thoroughly familiar with the method. The dangers inherent in injecting any hypnotic into the veins will prevent many surgeons from adopting the method, but these are said to be slight if proper precautions are employed. It is not suitable for long operations, and its chief advantages are in very brief procedures such as the opening of abscesses, removal of sutures, probing the nasolacrimal duct and discission in very nervous persons. While effective in children, the difficulties of intravenous injections in such cases, where the method would be especially convenient, are obvious.

Statti has summarized the advantages of *sodium pentothal*, a barbital derivative, as used by this method in 100 ophthalmic operations. He advises premedication with narcotics and the use of local anesthetics by instillation to minimize the amount of drug required. A 5 per cent solution is employed, of which 2 to 3 cc. is given by vein when everything is ready for the operation. In children or aged patients the initial dose is 1 to 2 cc. of the prepared solution. Anesthesia occurs in thirty seconds, when with the needle still in the

vein, amounts of 1 to 2 cc. of solution are given whenever signs of recovery occur. Most patients required 5 to 10 cc. (3 to 6 grains) before relaxation was complete enough for operation and received a total of 8 to 18 cc. for completion of the operation. Many of the operations performed were longer than those mentioned previously as being especially suitable for this method of anesthesia. In these shorter operations, a dose of 3 to 6 cc. should often be sufficient. Statti insists upon the necessity of giving oxygen or oxygen and carbon dioxide continuously during the operation as the respiration is always greatly depressed by the drug.

Sodium eripal, another barbital derivative, has also been employed for intravenous anesthesia in ophthalmic operations. Nizetic has reported on 115 operations in which it was employed without any alarming incidents. He injected 2 to 3 cc. of a 10 per cent solution at the rate of 1 cc. every thirty seconds as the initial dose. After sleep occurred, an additional 2 to 3 cc. was usually necessary for complete relaxation. The total amount required varied from 3 to 10 cc. Additional ether was necessary in only 6 cases.

In spite of all the improvements in local anesthesia, and such aids in its use as have been described, *general anesthesia by inhalation* will still be necessary in some ophthalmic cases. It is necessary in infants and may be preferred by some adults, especially for enucleation. Ether is still the anesthetic most employed in such cases, and its use in ophthalmic operations has been greatly facilitated by the introduction of the pharyngeal tube which obviates the use of the mask. In short anesthetics nitrous oxide or ethylene, besides being less unpleasant, is less apt to be followed by vomiting. With any general anesthesia fixation of the globe is necessary, and here the use of the bridle suture through the superior rectus has done away with one important difficulty. The use of morphine-atropine, or the hypnotics, before general anesthesia is as important as before operation under local anesthesia.

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CHAPTER III.

DRUGS AND ORGAN EXTRACTS USED IN OPHTHALMOLOGY.

PHARMACOLOGY OF DRUGS AFFECTING THE INTRAOCULAR MUSCLES.

THE effects of the atropine and pilocarpine groups of drugs have been known to pharmacologists for many years. It was known that after instillation of atropine dilatation of the pupil and paralysis of accommodation occurred and hence members of this group were called *mydriatics* and *cycloplegics*. Use of eserine and pilocarpine was followed by contraction of the pupil and spasm of accommodation and these drugs were called *miotics*. Recent work by Loewi, Dale, Cannon and others has greatly enlarged our knowledge of the exact location and mode of action of these drugs as well as of other drugs affecting the intraocular muscles. Out of these studies a working hypothesis has been formed which explains the reactions of muscles to stimuli by what is called the *chemical mediation of nerve impulses*. While a number of important details are still subjects of debate, enough links in the hypothesis have been given satisfactory experimental proof by these investigators so that their work constitutes an epoch-making advance in our knowledge. From the ophthalmologist's viewpoint important experimental work has been contributed by Wessely, Poos, Velhagen, Heath and Geiter and others, while Schoenberg and Guyton have provided especially useful reviews of the subject with deductions which are of practical importance to the ophthalmologist.

The hypothesis is based upon the proof that certain chemical substances are produced by stimulation of efferent nerves and that these substances are the agents which cause reac-

tion in the cells supplied by these nerves. These active chemical substances are not formed in the nerve trunks themselves but at two points, the synapse of preganglionic fibers in a ganglion and the end-plate of the postganglionic fiber on the surface of the innervated cell whether this be in a gland or a muscle (myoneural junction). The intrinsic muscles of the eye are innervated by parasympathetic and sympathetic fibers. There is evidence that the sphincter iridis, dilator iridis and ciliary muscles all receive fibers from *both systems, but it is known that active* contraction *of the* sphincter iridis and the ciliary muscle is produced in large part by stimulation of the parasympathetic and active contraction of the dilator iridis by stimulation of the sympathetic system.

Stimulation of the *parasympathetic nerve supply* to a muscle results in production of a substance both in the ganglion and at the myoneural junction which is *similar to and perhaps identical with acetylcholin.* This cholin derivative, which has been identified in the aqueous, chemically stimulates the smooth muscle cells to contract or, in the case of a gland, the glandular cells to secrete. Since the effect of parasympathetic stimulation is identical with that produced by direct application of this cholin derivative to the cell, the parasympathetic system has been called the *cholinergic system.* Drugs which produce an effect similar to that of parasympathetic stimulation or of direct application of acetylcholin may be called *parasympatho-mimetic* or *cholinergic drugs.* It will be seen that such drugs may act on various parts of the neuromuscular circuit. Acetylcholin is being produced constantly at all myoneural junctions supplied by the para-sympathetic system, and this constant supply is responsible for the tone of the muscles. Such a constant supply is necessary since the substance is as constantly being destroyed by a ferment, *cholinesterase,* which is produced by practically all tissues and is constantly present in the blood and tissue fluids.

It will be seen that increased activity of organs innervated by the parasympathetic system may be secured in several ways:

1. Central or peripheral stimuli may cause the production of more acetylcholin at the myoneural junctions.

2. An increased amount of this substance may be supplied through the general circulation, by local application or by local reactions such as result from inflammation or trauma.

3. Something may be done to destroy or inactivate cholinesterase, hence allowing the cholin-like substance already present to exert a cumulative effect.

4. The effector cells may be sensitized so as to give an increased response to the cholin-like substance already present.

5. The effect of opposing muscles innervated by the sympathetic system may be inhibited by various means.

Conversely, it is seen that lessened parasympathetic response may be brought about in several ways:

1. By decreasing the normal stimulation of the parasympathetic system, as by cutting or chemically paralyzing the nerve-trunks or ganglia.

2. By increasing the amount of cholinesterase. (Theoretical.)

3. By preventing access of the cholin-like substance to the muscle cells or in some way preventing its effect on these cells.

4. By causing actual paralysis or degeneration of the muscle cells.

5. By causing increased activity of opposing muscles innervated by the sympathetic system.

Stimulation of the *sympathetic nerve supply* to a muscle results in a somewhat more complicated process than that just described. At the synapse of a preganglionic fiber in the ganglion the same cholin-like substance is produced which is produced in parasympathetic ganglia. This allows the transmission of the nerve impulse to a postganglionic

fiber and through it to the end-plate in muscle or gland. Here, however, *a different substance is produced, which seems to be identical with epinephrine.* This substance does not directly affect the muscle cells, but acts by a more indirect method. The epinephrine so produced reacts with either of two substances which, though not as yet chemically isolated, must be assumed as present in the neighborhood of every cell innervated by the sympathetic system. One of these substances is present on the surface of cells which are *stimulated* to active contraction by the sympathetic system. Such cells are the smooth muscle cells of certain arterioles and of the dilator iridis. Combination of epinephrine with this substance produces the active substance known as *sympathin E,* which is directly responsible for *contraction* of the cells innervated. The other substance is present on cells of another type, whose reaction is *inhibited* by stimulation of the sympathetic system. Such cells are those of the sphincter iridis and probably also the ciliary muscle which, as has been stated, receive innervation from both the parasympathetic and sympathetic systems. Combination of epinephrine with this substance results in the substance known as *sympathin I,* which is directly responsible for *inhibition* or *relaxation* of the cells innervated. Assumption of these two substances, as a result of combination with epinephrine, is necessary to explain the contraction of certain muscles and relaxation of others after stimulation of the sympathetic system. It will be seen that the effect of stimulation of cells producing sympathin I will be to increase the effect of the opposing muscle cells which are predominantly innervated by the parasympathetic, while stimulation of cells producing sympathin E will lessen the action of such muscles by producing contraction of their opponents.

Since the effect of sympathetic stimulation is identical with that of epinephrine or adrenalin when applied to the cells directly the sympathetic system may be called the *adrenergic system.* Drugs which produce the effect of sympathetic

stimulation are known as *sympatho-mimetic* or *adrenergic* drugs. In the case of organs innervated by the sympathetic system, no esterase comparable to cholinesterase which destroys the active agent has been demonstrated, but its existence is postulated by some investigators (amine-oxidase).

It will be seen that, as in the case of the parasympathetic system, *increased reaction* of organs innervated by the sympathetic may be obtained by agents affecting various points in the circuit:

1. Central or peripheral stimulation of the sympathetic system will cause production of more epinephrine at the myoneural junction and hence, by reaction with the two substances already present, formation of increased sympathin E on the surface of certain cells and sympathin I on that of others.
2. An increased amount of epinephrine may be supplied systemically or locally, with the same end-result.
3. A theoretical amine-oxidase may be destroyed but nothing definite is known of such a mechanism.
4. The effector cells may be sensitized so that a given amount of epinephrine will produce a greater affect.
5. The effect of opposing muscles may be inhibited.

Also, *diminished reaction* of such organs may be accomplished in several ways:

1. By decreasing the normal sympathetic innervation, as by section or anesthesia.
2. By preventing the effect of sympathin on the effector cells.
3. By producing paralysis or degeneration of the cells themselves.
4. By stimulating contraction of opposing muscles.

The various drugs and other agents which affect the intrinsic muscles of the eye may now be considered, in so far as present knowledge permits, as regards the exact location of their effect on the myoneural mechanism. It may be seen

that every eye which comes under our observation constitutes a pharmacological laboratory in microcosm, in which each administrative detail must be considered if we are to utilize our therapeutic equipment most effectively.

PARASYMPATHOMIMETIC AGENTS—MIOTICS.
(See Fig. 15.)

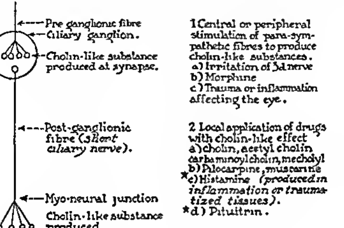
This includes all agents whose effect is similar to that of parasympathetic stimulation. While known as *miotics* from their predominant effect on the pupil, nearly all members of the group also *produce increased contraction of the ciliary muscle.* Although with certain drugs the increase in accommodation is slight in comparison with the miosis induced, this is apparently explained by the much greater concentration of drugs reaching the iris tissue when absorbed in the usual way through the cornea and into the aqueous, as compared with that reaching the ciliary body.

Figure 15 reviews the action of various agents, not only drugs but also physical agents and the products of inflammation, which produce contraction of the iris and ciliary body.

The miotic effect of morphine and its derivatives when given systemically is well known. These drugs may be placed in Group I since they affect the pupil by central stimulation of the parasympathetic system.

Pilocarpine, included in Group 2 of Figure 15 acts, so far as is known, directly on the smooth muscle cells. It behaves like the cholin derivatives with the important difference that it is stable and is not destroyed by cholinesterase. Hence its effect is much more prolonged. A drop of 1 to 3 per cent pilocarpine nitrate or hydrochloride when instilled in the conjunctival sac will produce miosis beginning in about ten minutes and persisting approximately twenty-four hours. The 1 per cent solution is usually employed to counteract the effect of cycloplegics and in chronic glaucoma. In this concentration some effect on the normal ciliary body is

produced, but it is not so marked as after the use of eserine. Hence the symptom of painful ciliary spasm is less often noted while, after cycloplegics, accommodation is not restored to normal so rapidly as when eserine is employed. Prolonged use of the drug causes sensitization, as evidenced by symp-



* See discussion on page 52.

Fig. 15.—Mode of action of the parasympatho-mimetic agents

toms of irritation and the formation of follicles in the conjunctiva. For the use of pilocarpine and other drugs in glaucoma, see page 298. Muscarin and arecoline, while chemically allied to pilocarpine, do not appear to have been employed in ophthalmology.

Cholin Derivatives.—The chemical value of the cholin derivatives is limited by the rapidity with which they are destroyed in the tissues by cholinesterase. Destruction is practically immediate in the case of *acetylcholin*. *Acetylbetamethylcholin chloride,* known as *mecholyl,* is slightly more stable but must be used in concentrated solutions. Clarke has employed it in 10 and 20 per cent solutions by instillation and in doses of 0.025 gm. by retrobulbar injection, in cases of acute glaucoma, with good results. Even better results were obtained by its use as a synergist with prostigmine. (See page 53.) Another cholin derivative, *carbaminoyl-cholin,* known as *doryl,* is the most stable drug of the group. It has been advocated by Velhagen in chronic glaucoma. A 0.75 per cent solution was found to be a more active miotic than 2 per cent pilocarpine and slightly less active than 1 per cent eserine. Because of its greater stability, it may prove to be more useful than mecholyl as a synergist to miotics of the eserine-prostigmine group. Swan has recently shown that absorption of doryl varies greatly when it is used in aqueous solution. By employing solutions of 1 to 300 zephiran as a vehicle, sufficient lowering of the surface tension was produced on the cornea to allow prompt uniform absorption. A 1.5 per cent solution of doryl in this vehicle was found to have a much more marked and prolonged effect, both on the pupil and on intraocular tension, than a 2 per cent solution of pilocarpine. To this group should be added a preparation recently described by Myerson and Thau (1940). This is furfuryl trimethyl ammonium iodide which they found, in 5 to 10 per cent solutions, to be a powerful parasympatho-mimetic agent, the most powerful, they state, with which they had experimented. They noted a peculiar difference between its effect and that of other drugs in the group, namely that the anterior chamber became shallow after its use, apparently due to extreme ciliary spasm, while the tension was lowered 8 to 10 mm.

Their work was conducted on normal subjects and as yet no reports on use of the drug in glaucoma have appeared.

For the use of this group of drugs in producing vasodilatation, see page 92.

Histamine and Pituitrin, while listed in Group 2, because of their direct stimulating effect on smooth muscle, differ from the cholin derivatives and pilocarpine in certain respects. Their effect is not prevented by atropine and hence, according to Dragstedt,* is not dependent on the special substance known to be present in the cells which reacts with typical drugs of this group to produce muscular contraction. The effect seems to be a direct one on the muscle cells. Histamine, whether applied locally in the form of a 10 per cent solution (Aminglaukosan-Hamburger) or produced in the tissues as a result of inflammation or trauma, is an extremely powerful miotic. The marked edema and congestion resulting from its use form a contraindication except under very special conditions. Pituitrin has a feeble miotic effect, but has been shown to reduce intraocular tension when 0.3 to 0.5 cc. of the standard obstetrical solution is injected subconjunctivally (Samojloff).

Eserine and Prostigmine.—These drugs are the best known examples of Group 3 in our table. Because of the carbamate (urethane) group in their structure, they inactivate cholinesterase, and this effect is so complete and prolonged as to result in marked miosis and ciliary spasm. *Eserine* (physostigmine) is usually employed as the salicylate or sulphate in solutions of 0.2 to 2 per cent. The 0.2 per cent solution is usually considered equivalent to 1 per cent pilocarpine and is employed in chronic glaucoma and to neutralize the effect of a cycloplegic. The ciliary spasm produced is much more intense than that of 1 per cent pilocarpine, however, and often very annoying. Hence pilocarpine is preferred, as a rule, after cycloplegia. Conjunctival reactions and dermatitis occur more frequently after prolonged use of eserine

* Personal communication

to sympathin E. It has been used in glaucoma, usually by the subcutaneous route. It usually produces no change in the pupil when given by this route.

SYMPATHO-MIMETIC AGENTS—MYDRIATICS AND CYCLOPLEGICS. (Fig. 16.)

This name is used to describe all agents whose effect is similar to that of sympathetic stimulation. Figure 16 which attempts to group these agents is necessarily more complicated than the previous table, because of the two kinds of cells innervated by the sympathetic, whose myoneural junctions produce, respectively, the effector substance, sympathin E and the inhibitor substance, sympathin I. The most important effects of the sympatho-mimetic agents on the intraocular muscles are concerned with cells producing the effector substance in the dilator iridis. The effect of these agents is, in general, reinforced by the fact that the same agents also affect cells in opposing muscles which receive only inhibitor fibers from the sympathetic. This is true of the sphincter iridis which partially relaxes under sympathetic stimulation, and probably also of the ciliary muscle. (Poos.)

There are no important drugs which need be included in Group 1 of the table.

Epinephrine, the active substance which reacts with sympathin E and sympathin I, is the typical agent included in Group 2. Aside from its principal effect of producing contraction of the dilator iridis, it also produces relaxation of the sphincter and probably also of the ciliary muscle. In the usual 1 to 1000 solution it produces demonstrable mydriasis in only a few persons when instilled in the sac. When placed on a pledget beneath the upper lid, however, or injected subconjunctivally, a marked mydriasis is produced in normal eyes, while in cases of iritis the mydriasis may be so active as to rupture fresh inflammatory synechiæ, even in cases which were resistant to atropine. The effect is much less prolonged than that of atropine, persisting for several

hours in normal eyes, but for a shorter time in inflamed eyes. It may be made to persist longer by the subsequent use of atropine, but in severe iritis the pupil often contracts within a few hours in spite of atropine. The same effect may be conveniently secured by preparations of epinephrine which

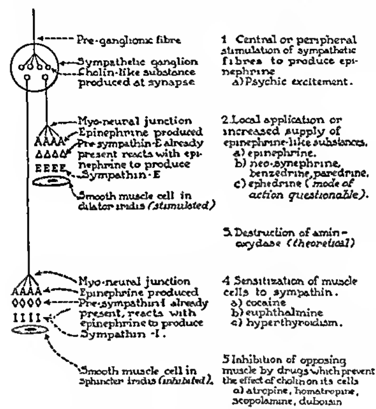


FIG. 16.—Mode of action of the sympatho-mimetic agents.

are effective on instillation in the conjunctival sac. One per cent adrenalin chloride, 2 per cent suprarenin bitartrate (Green), and 2 per cent suprarenin bitartrate jelly (Alvis) are satisfactory preparations. These are synthetic preparations of levo-rotatory epinephrine. The same is true of the

German proprietary preparation known as Laevo-glaukosan (Hamburger). This is a 2 per cent solution with an almost inactive by-product, and is probably no more effective than the former preparations. With these solutions the danger of systemic reactions is very slight, but it is well to compress the naso-lacrimal duct for five minutes after their use to minimize systemic absorption.

Epinephrine Substitutes.—Identical with epinephrine in their mode of action are a number of synthetic substances of allied chemical structure. These include benzedrine, paredrine, and neosynephrine. The use of benzedrine in refraction has been described by Myerson and Thau and by Beach and McAdams, that of paredrine by Tassman, while the effects of neosynephrine have been studied especially by W. Post and by Heath and Geiter. A number of other reports have appeared. All of these drugs when used in suitable concentration produce mydriasis and paralysis of accommodation which is less complete than that of atropine and which persists only from two to six hours. No appreciable rise in tension was seen when the drugs were employed in normal persons. The effect on accommodation may be explained as due to stimulation of sympathetic nerve endings in the ciliary muscle which produce sympathin I and hence inhibit this muscle, but other theories have been advanced.

Benzedrine and paredrine have been employed chiefly as synergists of atropine and homatropine in refraction with the object of lessening the amount of the atropine derivatives necessary to produce cycloplegia and hence of shortening the resulting period of disability. Another advantage claimed is the rapidity with which mydriasis for fundus examination may be produced. Various combinations of the drugs have been employed. Beach and McAdams employed 1 drop of 1 per cent benzedrine sulphate with 1 or 2 drops of 5 per cent homatropine hydrobromide in adults and of 1 per cent atropine in small children. Tassman preferred paredrine because he believed it was less irritating, employing 1 drop

each of 1 per cent paredrine hydrobromide and 4 per cent homatropine, or 1 per cent atropine depending on the age of the patient. Weinman and Fralick found that the disability from cycloplegia was considerably less prolonged when 2 drops of 1 per cent benzedrine or paredrine with 2 drops of 5 per cent homatropine were employed than after homatropine alone. They compared the effect, however, with that of 6 drops of 4 per cent homatropine with 0.5 per cent cocaine and this solution is stronger than that usually employed. They found paredrine to be slightly less irritating than benzedrine. Thorne and Murphey have compared these methods with the use of 5 per cent homatropine hydrobromide alone. They conclude that practically identical effects are produced by 1 drop each of 5 per cent homatropine and 1 per cent benzedrine, 6 drops of 2 per cent homatropine and 1, 2 or 3 drops of 5 per cent homatropine. The quickest recovery from cycloplegia was observed after 1 drop of 5 per cent homatropine.

There is no doubt that satisfactory cycloplegia may be secured by members of the atropine group alone when properly employed. Hence, the conclusion seems justified that benzedrine and paredrine are of use chiefly in producing rapid mydriasis for ophthalmoscopic examination and that their use with homatropine or atropine for refraction, while it may possibly permit satisfactory refraction with a minimal amount of the atropine derivatives and with fewer instillations, need not as yet be accepted as a necessary addition to the routine of refraction.

Neosynephrine, while producing almost the same effects as benzedrine and paredrine, has been used chiefly for its decongestive and mydriatic effects. Like the two former drugs it is stable for long periods even in high concentration, in which it offers a great advantage over epinephrine itself. A 1 per cent solution was shown by Heath to prevent the edema produced by mustard oil, and the author and his associates have observed rapid absorption of conjunctival edema

following instillation of 1 and 10 per cent emulsions. Angioneurotic edema of the lids subsided rapidly when the 10 per cent emulsion was massaged into the skin of the lids. The advantage of the water in oil emulsion of neosynephrine, as described by Heath, is that it adheres to the cornea and conjunctiva, allowing more prolonged absorption of the drug. The mydriasis produced by neosynephrine is prompt and active, the 10 per cent emulsion being apparently more efficient than any other preparation tried by the author in the dilation of pupils resistant to atropine. (See Fig. 17.) The effect on accommodation is definite but slight. Occasional slight increases of tension were observed by W. Post, but these were never marked, while in most cases the tension was lowered 4 to 5 mm. In two eyes with initial tension of 30 to 32 this drop in tension amounted to from 11 to 13 mm. No extensive observations seem to have been reported on its use in glaucoma, although it should theoretically have the same effect as epinephrine.

Ephedrine, while chemically related to epinephrine, differs from it in some particulars as regards its mode of action. Its effect is not increased by the previous use of cocaine as is the case with epinephrine and hence it may be supposed to act in a different manner. It has been suggested that ephedrine may destroy a theoretical amin-oxidase (Group 3) but there is no definite proof of this and hence the drug has been tentatively placed in Group 2 of the outline.

A 3 per cent *solution of ephedrine* has been *employed to* dilate the pupil for ophthalmoscopy, and is reasonably effective. Its decongestive effects are well known and may be employed under certain conditions. A peculiar effect of ephedrine when given systemically is to stimulate the higher centers so as to produce temporary relief from somnolence. In true cases of narcolepsy, in which inability to use the eyes is common, this property of ephedrine has been used with almost specific effect. The oral dose in such cases is $\frac{3}{8}$ to $\frac{3}{4}$ grain repeated two to three times a day. Benzedrine

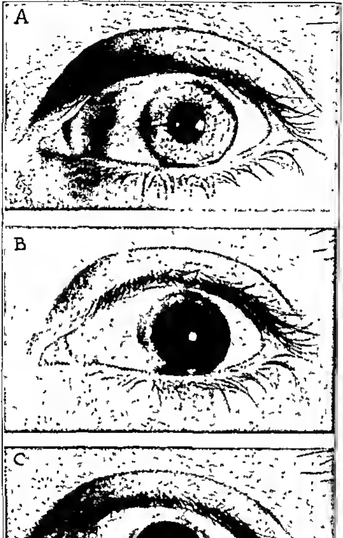


Fig. 17.—Effect of sympatho-mimetic drugs on the pupil. *A*. Normal pupil. *B*. Pupil after 2 per cent **homatropine**. *C*. Pupil after 10 per cent neosynephrin.

sulphate is probably even more effective in doses of 5 and 10 mg. The use of these drugs is not without the danger of occasional systemic reaction, and should not be advised without careful observation and control of dosage.

The principal examples of drugs placed in Group 4, which act by sensitizing the muscle cells to sympathin are cocaine and an allied derivative of beta-eucain, known as euphthalmine. These drugs, in the concentration commonly employed, produce moderately active mydriasis, with slight decrease in accommodation. Both effects are relatively brief as compared with that of the atropine derivatives. An objection to cocaine is its effect on the corneal epithelium which is practically absent with euphthalmine. Hence euphthalmine in 3 to 5 per cent solution has been commonly employed for examination of the fundus and retinoscopy in patients past the age of forty-five. No increase in tension is usually observed after euphthalmine, but in rare cases an acute attack of glaucoma may be precipitated by this drug, and the use of a miotic after the examination is definitely indicated.

Atropine and Its Derivatives.—The most important group of sympatho-mimetic drugs is discussed last, as its mode of action places it in Group 5. The statement is usually made that these drugs act by paralyzing the sphincter iridis and ciliary muscle. For practical purposes this is true. Actually, however, the muscle fibers are not paralyzed by atropine, as they respond to direct stimulation and to certain agents such as histamine. The atropine group does, however, act upon the myoneural junction in such a way as to prevent access of the cholin-like activating substance to the muscle cells or to make these cells refractory to its effect. This occurs when minute amounts of these drugs reach the muscles and hence, in the solutions usually employed, they can be relied upon to produce mydriasis and cycloplegia of a degree satisfactory for refraction. All members of this group act in the same way, the differences being chiefly in the duration of the effect.

Atropine, most powerful of the group, produces, in the usual 1 per cent solution of the sulphate, mydriasis which begins within fifteen minutes and persists for ten to fourteen days. Cycloplegia begins within twenty-five minutes and persists for a variable length of time, its depth and duration depending upon the activity of the ciliary muscle. Since this is much greater in infancy and childhood, it requires repeated instillation to produce complete cycloplegia in very young children and the effects pass off within two to three days. In normal adults one or two instillations produce practically complete cycloplegia, which persists for three to five days, considerable inconvenience in reading being noted for ten to fourteen days in certain persons. In cases showing iris irritation, especially in iritis, the effects on both the iris and ciliary body are especially brief and several instillations per day are often necessary to maintain mydriasis and some degree of cycloplegia.

Because of these properties, atropine is employed for refraction, as a rule, in infants and children to the age of ten to twelve years, while one of the weaker substitutes is preferred in older persons. In a few adults with marked ciliary spasm atropine is necessary for accurate results, and in such cases each eye is usually refracted separately with an interval of at least two weeks, as in this way complete inability to read is avoided. Between the ages of ten and fifteen years the response to cycloplegics varies considerably, but it can usually be determined by retinoscopy under a weaker cycloplegic whether paralysis of accommodation is complete, and if it proves not to be, atropine may then be employed. The amount of atropine employed for routine refraction varies among different ophthalmologists. In order to be fairly sure of complete cycloplegia, a common procedure in children under twelve years is to order a drop of 1 per cent atropine instilled in each eye three times a day for three days, refraction being performed on the third day. Less than this may be sufficient in children between ten and twelve years, espe-

cially in myopes, while more may be necessary in smaller children, especially those who are hyperopic. In cases involving inflammation of the uveal tract such as iridocyclitis, keratitis, scleritis and injuries of the eye, the use of atropine is of the greatest importance. If used very early, it prevents posterior synechiæ from forming, while in later cases it minimizes their extent. In any case cycloplegia and mydriasis produce definite relief from pain and congestion. After most intraocular operations atropine is employed to prevent or minimize postoperative irritation of the iris and ciliary body. When employed for inflammatory conditions, solutions stronger than 1 per cent may be necessary; 2 to 4 per cent solutions, 2 per cent ointment, or even a minute crystal of the drug itself placed in the conjunctival sac may be employed. The use of atropine in synergy with drugs of the epinephrine group is often successful in dilating pupils which have resisted atropine alone. Various combinations which may be employed will be discussed on page 277.

Atropine *should never be used for ophthalmoscopic examination* except in infants whose pupils do not react to weaker derivatives.

In using atropine several precautions must be observed. It must be remembered that 1 minim of 1 per cent solution contains $\frac{1}{100}$ grain of atropine sulphate, and that a large part of this finds its way by the naso-lacrimal duct into the nasopharynx, where it is absorbed into the circulation. *Hence in babies it must be used with caution,* as fatalities have been observed following absorption of atropine in this way. If pressure is made over the lacrimal sac for two to three minutes following instillation most of the drug will escape with the tears upon the face. When atropine is given for home use by the parents of babies this precaution must be observed, or a weaker solution, 0.2 to 0.5 per cent, should be prescribed. Since atropine causes a rise of intraocular tension in cases of glaucoma, *one should be sure that the tension is not elevated before it is given,* except in cases where the pupil is bound down. Where one is in doubt as to the diagnosis

of iritis or cyclitis it is well to attempt dilatation of the pupil with homatropine, as the disability resulting from atropine may be avoided. The same is true in cases of very mild iritis or small infiltrations of the cornea, where the pupil is easily dilated with homatropine, as it may only be necessary to maintain mydriasis for a few days in such cases. The continued use of atropine produces in certain persons a definite conjunctivitis, in which the appearance of the conjunctiva resembles greatly that in trachoma. A dermatitis is

FIG. 18 —Dermatitis and conjunctivitis due to atropine.

also frequently present. (See Fig. 18.) To avoid this, the amount of atropine used must be cut down as soon as the condition of the eye warrants this, and one should be on the watch for signs of conjunctival irritation as, when these occur the drug must be stopped at once. If mydriasis is still desirable, one of its substitutes must be used.

Homatropine, employed as the hydrobromide, is the member of the atropine group *most employed in refraction.* Mydriasis following its use persists for twelve to twenty-four hours. Cycloplegia passes off sufficiently to permit reading after six to ten hours, although some effect persists for ten to twenty-four hours. A 2 per cent solution is usually em-

ployed, 5 drops at ten-minute intervals producing satisfactory cycloplegia in most persons past the age of twelve years within one hour after the first drop. One drop of 5 per cent solution produces an equal effect, but the use of 2 drops is more certain as part or all of a single drop may be expelled before absorption has occurred. It is true, as Bothman and others have shown, that cycloplegia with homatropine is not complete, from 0.7 to 1 diopter of accommodation remaining in most cases after one hour. This amount, however, does not interfere with retinoscopy at 1 meter nor with subjective refraction at the 20-foot distance. The advisability of using benzedrine or paredrine as synergists to homatropine and atropine has been discussed. (See page 56.) In ophthalmoscopic examination 1 drop of 2 per cent solution is usually sufficient.

The same dangers are involved in the use of homatropine as with atropine, but these may be more easily counteracted or avoided. Acute attacks of glaucoma have been brought on after using homatropine in refraction. This is especially to be feared in persons above the age of forty years, but may also occur in younger patients. Although there must exist a predisposition to glaucoma in such cases, it is impossible to diagnose such a predisposition beforehand, and *the only safe procedure when using homatropine in refraction is the use of a miotic immediately afterwards* for all patients except children. In high myopes, where miotics may be considered dangerous, this may usually also be dispensed with. In persons above the age of twenty-five years it is certainly safest, besides the use of a miotic once in the office, to dispense a small amount of the miotic for use once or twice before retiring on the day of the refraction. Abraham, in a recent survey, found records of only 26 cases of "mydriatic glaucoma" developing in persons without previous signs of glaucoma. Only 4 of these were in persons below the age of thirty years. He concludes that the use of a miotic after cycloplegia is not necessary under the age of twenty years. Systemic effects from homatropine are seen

occasionally in young children and susceptible persons. They consist in dryness of the mouth, flushing of the skin, fever and nausea, but are seldom severe and, so far as the author knows, never fatal. They may be prevented by instructing patients to make pressure over the lacrimal sac for three minutes following each drop. Conjunctivitis from homatropine seldom occurs, probably because the drug is seldom used for long periods.

Hyoscine, the levo-rotatory isomer of scopolamine, is intermediate in its effects between atropine and homatropine It produces effective cycloplegia in more dilute solutions, 0.2 to 0.5 per cent of the hydrobromide being commonly employed, but the duration of cycloplegia is not so long as after atropine, only about two days. It is used by some ophthalmologists in refraction, but has the disadvantage that some persons notice a marked psychic disturbance when small amounts are absorbed. Hence special precautions to close the lacrimal passages are necessary when it is employed. It is an exceedingly useful substitute for atropine in patients with inflammatory conditions who develop an idiosyncrasy to atropine. A few patients become sensitized to this drug as well, and in such cases another substitute must be employed.

Duboisin sulphate has about the same cycloplegic and mydriatic effect as scopolamine and is used under the same conditions but in 0.5 to 1 per cent solutions. (Hyoscyamine is a drug chemically identical with duboisine but it is obtained from a different source.)

Atropine methylnitrate (eumydrine) and **atropine methylbromide** (mydriasine) have, according to Guyton, effects similar to scopolamine, but are not permissible in cases of atropine sensitivity.

PRESERVATION OF DRUGS USED FOR INSTILLATION.

Since most drugs used for instillation contain their salts or alkaloids in relatively weak concentration, yeasts and fungi grow in these solutions, unless some preservative is added.

Forty grains of boracic acid crystals added to the ounce makes a supersaturated solution in which fungi do not grow and which remains clear indefinitely if ordinary precautions are taken to keep it clean. The addition of the crystals does not interfere with the action of most drugs and is said to make some drugs, such as cocaine and hutyn, less irritating by converting them to the horate. It is unnecessary in solutions of mercurochrome, silver nitrate, mercuric cyanide and other antiseptics in stronger solutions. For some reason 1 to 1500 mercuric cyanide is usually used to preserve dionin, and the same preservative is preferred hy many opthalmologists for other solutions. *A grain of camphor or menthol to the ounce or 0.5 per cent of chlorctone* are also effective preservatives. Eschenbrenner has described the use of benzoic acid esters for the preservation of eye drops, and Hasler has reviewed the reasons for considering certain combinations of these esters the ideal preservative. P-oxybenzoic acid methyl ester, known as Nipagin-m, is mixed in its powdered form with P-oxyhenzoic acid, propyl ester known as Nipasol-m in the proportion of 65 of the former to 35 of the latter.

Eight-tenths (0.8) gram of this combination per liter of distilled water is used as the solvent in making up solutions of the common alkaloids and local anesthetics. The preservative in this strength prevents the growth of molds and bacteria in solutions, and is without color, odor or irritating properties. It does not interfere with the soluhility or effectiveness of the drugs employed and the prevention of mycotic growth preserves the alkaloids in an unchanged chemical state for long periods.

REACTION AND OTHER FACTORS AFFECTING DRUGS USED FOR INSTILLATION.

Besides the properties of the drug used for instillation, *the medium in which it is given may itself affect the resulting irritation, speed of absorption and ultimate therapeutic effect of the drug.* Solutions isotonic with the body fluids will be

less irritating than strongly hypertonic or hypotonic solutions. Lipschütz found, however, that a more important factor in causing irritation is a variation toward *acidity or alkalinity of the solution*. Sodium chloride solutions from 0.3 to 1.5 per cent caused no feeling of irritation when kept at the neutral point, while an isotonic solution, if markedly acid or alkaline, caused severe irritation. Normal saline at a pH from 8 to 7 caused no sensation. At pH 9 a slight feeling of irritation was produced, while on the acid side solutions at pH 6.6 to 6.3 caused a slight feeling of dryness and those at pH 6 to 4.5 severe burning. The tears are hypertonic, containing slightly more than 1 per cent sodium chloride and are alkaline, with a pH of 8.

Most of the alkaloids are employed in the form of their soluble salts which gives their solutions an acid reaction. The pH of some of the common alkaloids and metal salts used in ophthalmology, in distilled water, was found by the author to be as follows: 1 per cent atropine sulphate, 5.8, 2 per cent homatropine hydrobromide, 5.5; 2 per cent cocaine hydrochloride, 4.6; 1 per cent pilocarpine nitrate, 4.8; 0.2 per cent eserine sulphate, 6.6; 4 per cent novocaine hydrochloride, 4.6; 2 per cent butyn sulphate, 5.4; 0.9 per cent sodium chloride, 7; 0.2 per cent zinc chloride and boracic acid, saturated solution, 4.2.

The fact that a saturated solution of boracic acid causes but slight irritation indicates that this acidity alone cannot be made responsible for irritation in solutions of all drugs, as might be deduced from the work of Lipschütz. All the drugs used in a saturated solution of boracic acid showed reactions from pH 4.2 to 5. The slight irritation of such solutions, however, is a cause of complaint by some patients, and the use of neutral solutions when possible will obviate this.

There are other reasons for controlling the reaction of solutions employed. Certain drugs are soluble only within certain limits of reaction. *The zinc salts are precipitated in alkaline solutions and made inactive.* To have any effect

on the conjunctiva, according to Lipschütz, they must be used in acid solutions of pH 5.5 which will protect them from immediate precipitation by the tears. *Holocaine is only soluble in solutions as acid as pH 4.8,* while *butyn, cocaine and adrenalin, soluble in distilled water, are precipitated in salt solutions less acid than pH 5.9. Metaphen and fluorescein are soluble only in alkaline solutions of about pH 9,* while uranin, a soluble salt of fluorescein, is soluble in distilled water and, probably for this reason, is less irritating. The absorption of alkaloids by the cornea, which accounts for nine-tenths of the amount absorbed, is, according to Fischer, markedly affected by their reaction. He found that pilocarpine was absorbed best at pH 4 to 5, while for atropine, scopolamine and eserine the optimum reaction was pH 7.5. Such differences in absorption will naturally alter materially the effect produced.

A series of buffer solutions is easily made in which alkaloids can be maintained at any desired reaction. The following solutions were chosen because of the simplicity by which a suitable range of reactions could be obtained and because the amount of boracic acid contained in them proved to prevent growth of molds and bacteria for long periods. They can be made by any good pharmacist providing the anhydrous form of the salts is employed, the materials are weighed carefully, and chemically clean glassware, including pipettes graduated to $\frac{1}{10}$ cc. are employed. Two solutions are made up in amounts of one to several liters and by mixing these solutions of the desired reaction between pH 5 and pH 9 are obtained. Acid Buffer Solution No. 1 contains:

Boracic acid	12.4 gm.
K Cl (anhydrous)	7.4 gm.
Distilled water	1000 cc.

Stock Sodium Carbonate Solution contains:

Na_2CO_3 (anhydrous)	21.2 gm.
Distilled water	1000 cc.

This solution is employed in very small quantities for making other solutions and *should never be employed in its concentrated form* as a solvent for drugs used in the eye.

Acid buffer solution as described has a pH of 4.8 to 5, and is a suitable medium for butyn and holocaine salts. For the latter it should be warmed slightly before the drug is added, when it will remain in solution without addition of further acid. This solution is necessarily slightly irritating, but in the case of holocaine this cannot be avoided, while butyn in distilled water has n reaction almost as acid. (pH 5.4.) It is not noticeably more irritating in this solution and remains clear longer than in water.

Acid Buffer Solution No. 2, of reaction pH 6, is obtained by adding 0.05 cc. of stock sodium carbonate solution to 30 cc. of Acid Buffer Solution No. 1. This is suitable for the zinc salts and for cocaine and epinephrin.

Alkaline Buffer Solution No. 1, of reaction pH 7.0, is made by adding 1.5 cc. of stock sodium carbonate solution to 30 cc. of Acid Buffer Solution No. 1. This is suitable for most of the alkaloid salts, especially those of atropine, homatropine, scopolamine, pilocarpine and eserine. In this solution they are less irritating than in distilled water, as all of them have an acid reaction, and less than in the saturated solution of boracic acid. There is some evidence that most of them are absorbed better in this slightly alkaline solution. In the case of pilocarpine, in spite of Fischer's experimental work previously mentioned, clinical tests seemed to show that its effect on the pupil was at least as rapid in this solution as in the acid solution he advised. Solutions of eserine in this medium turn pink rapidly, but their effectiveness is not impaired by this change, in spite of a general opinion to the contrary. While marked idiosyncrasies to the alkaloids cannot be prevented by any medium, there is some evidence that milder but unpleasant reactions occur much less frequently when the drugs are employed in this alkaline solution. This buffer solution itself has proven to be a useful

and non-irritating collyrium in cases requiring a substitute for tears. (See Chapter VIII.)

When a more alkaline solution is desired, as to dissolve the secretion in vernal conjunctivitis, Alkaline Buffer Solution No. 2, of pH 8.4, is obtained by adding 4 cc. of stock sodium carbonate solution to 30 cc. of Acid Buffer No. 1. A 3 per cent solution of sodium bicarbonate has a similar reaction and may be employed for this purpose if the buffer solutions are not available.

For dissolving sodium fluorescein a still more alkaline solution is necessary, of pH 9. This is obtained by adding 8 cc. of stock sodium carbonate solution to 30 cc. of Acid Buffer No. 1.

Correspondence with ophthalmologists, pharmacists and manufacturers has brought out certain facts as to the solubility of various drugs and their compatibility with the buffer solutions. The manufacturers of *Euphthalmine* advise against Alkaline Buffer No. 1 as a medium for that drug, stating that it would be decomposed by sodium carbonate. They suggest the following medium:

Boric acid	12.4 gm.
Sodium borate	0.5 gm.
KCl	7.4 gm.
Aqua dest. q. s. to	1000.0 cc.

This solution, when mixed with an equal volume of 10 per cent solution of euphthalmine in distilled water, has a pH of 5.9 compared with a pH of 4.815 for the 10 per cent aqueous solution alone and 4.88 for the 5 per cent solution. Miss Edith Heister of Cincinnati has dispensed the drug in this solution and believes it to be very satisfactory.

Phenacaine (holocaine) is insoluble in Acid Buffer Solution No. 1 when cold, but is brought into solution by warming and seems to remain in stable solution in this medium after cooling for considerable periods.

Paredrine, according to the manufacturers, is not stable at a pH above 6.0, but there seems to be no reason why it

cannot be used in acid buffer No. 1 or No. 2 if desired. Bellows found that a combination of 5 per cent homatropine and 2 per cent *paredrine was soluble in the above buffer* solutions from pH 4.6 to 8.75 and that these alkaloids produced only a slight effect on the reaction of the solutions, the change being plus 0.15 in acid buffer No. 1 and minus 0.05 in alkaline buffer No. 1, a change too slight to affect the irritating properties of the solutions.

For reasons previously stated, no attempt was made to make the buffer solution isotonic with the tears. Mr. Leonard Seltzer of Detroit has pointed out, however, that the four solutions most commonly employed happen to approach fairly near to isotonicity. Using Nicola's method of computation, he finds their sodium chloride tonicity equivalent to be as follows:

Acid Buffer No 1	5 1522
Acid Buffer No 2	5 15223
Alkaline Buffer No 1	5 18787
Alkaline Buffer No. 2	5 2405

These figures may be compared with 6.356, the tonicity equivalent of the lacrimal secretion expressed in grams of sodium chloride to the ounce of distilled water necessary to make a solution isotonic with the tears. Mellen and Seltzer have *shown how, using Nicola's tables, the proper amount of* sodium chloride may be added to ophthalmic solutions to make them isotonic with the tears, allowance being made for the effect on tonicity of the salts and alkaloids commonly employed. In using buffer solutions as media for alkaloids and astringents the author feels that this additional refinement is seldom required, although it may be tried for patients who complain of all the ordinary solutions. In the case of solutions to be employed with contact glasses, however, the method employed by Seltzer may prove to be of considerable practical importance.

In certain damp climates, as Hasler has shown, the boracic *acid present in these buffer solutions is insufficient to pre-*

vent the growth of molds. Hence he has made the useful suggestion of substituting for the distilled water employed in the stock solutions a solution of 0.8 gm. Nipagin-Nipasol (see page 66) in 1000 cc. of distilled water. This will give a concentration of about 0.08 per cent in the resulting buffer solution which he found perfectly effective in preserving solutions in the climate of the Pacific coast. Bellows found that 0.04 per cent nipasol produced no effect on the pH of the buffer solution and the same was true of chloretone in 0.5 and 1 per cent solutions. An inconvenience which he noted when employing chloretone was its poor solubility, which necessitated warming or filtering the solution. When a buffer solution as alkaline buffer No. 1 is used as a collyrium without an added preservative, it is advantageous to dispense a fairly large amount in a screw-cap container, which is kept in the refrigerator. The one-half ounce dropping bottle used by the patient is filled at intervals from the larger bottle, which greatly lessens bacterial contamination.

A medium for antiseptics such as metaphen which presents certain advantages is 3 per cent gelatin, as proposed by R. D Smith. Such a solution spreads in a thin film over the conjunctiva and keeps the drug in contact with it longer than is the case when a watery solution is employed. Alkaloids may also be used in gelatin solution, but a preservative must be added as it is otherwise an excellent medium for bacteria. The use of water in oil emulsions has been employed to advantage by Heath in the case of neosynephrine, which is absorbed most effectively through the cornea when used in this medium.

EXTRACTS OF THE GLANDS OF INTERNAL SECRETION.

The diagnosis and treatment of endocrine disorders is in an early stage of development. Enthusiasts have employed extracts of little or no biological potency in all sorts of conditions with claims of extraordinary results. Ophthalmolo-

gists have shared in some of these enthusiasms and the literature in this field has been filled with confusion. Within recent years potent extracts, biologically standardized, have been made from a number of glands, and progress has been made in the more exact diagnosis of endocrine disorders. In the following notes an attempt is made to discuss *the ophthalmological conditions in which endocrine imbalance is definitely known to be an important factor,* with brief mention of other conditions in which various types of endocrine therapy have been employed. Some of these hormones produce active pharmacodynamic effects on the intraocular muscles which have been previously discussed.

Glandular Extracts.

Thyroid Extract and Thyroxin.—This hormone is known to increase basal metabolism, increase the heart-rate, raise the blood-pressure and lower blood cholesterol when given systemically, usually by mouth. *It should only be employed in persons with a lowered basal metabolic rate and in dosage only sufficient to raise the rate to normal.* It has been employed in various ocular diseases including myopia, keratoconus and chronic uveitis. There seems to be no definite evidence of its value in the two former conditions, and any value it may have in chronic uveitis would seem to be by restoring normal metabolic processes in tissues which were functioning abnormally, as a result of which the body's defense mechanisms against infection may be increased in efficiency. In certain degenerative conditions associated with high blood cholesterol and myxedema the systemic use of thyroid extract is of definite value. Lebensohn has reported the use of thyroid extract in small doses, $\frac{1}{2}$ to 1 grain a day, in a series of cases with *intractable asthenopia.* These patients showed a slightly reduced basal metabolism and their symptoms, as a rule, were greatly relieved when this was brought to normal. It is not known how frequently a lowered metabolism occurs in such cases, but it is a factor which may be considered in

patients whose symptoms have resisted other measures. It is certainly a good rule, however, that thyroid should not be given without a record of basal metabolism and only in cases in which it is shown to be below normal.

The local use of thyroxin, as suggested by Jamieson in certain forms of chronic conjunctivitis and even in incipient cataract, is based upon an entirely unproven idea that an effect on local tissue metabolism can be produced in this way. Definite clinical evidence of any benefit from such local applications seems to be lacking.

Gillette has carefully checked the lens changes in 20 patients who instilled a solution of thyroxin daily for thirteen to fifty-seven months, and found no improvement in the opacities in any case. Progress in the lens opacities occurred in most cases as it did in a series of untreated cases.

Parathyroid Hormone.—The only indication for this hormone is in tetany parathyreopriva, which is often accompanied by cataract. It is probable that early administration of the hormone will prevent the development of cataract in some cases of tetany following thyroidectomy and that it may stop the progress of this type of cataract if given before marked lens opacities have developed. The dose advised is 10 to 25 units a day, but this must be regulated by records of the blood calcium. Enough hormone should be given to keep the blood calcium at 10 to 11 mg. per 100 cc.

Insulin.—The value of insulin in diabetes is too well known to require comment. It is of value, of course, in the ocular complications of diabetes, such as diabetic retinopathy and recurrent hemorrhages in the vitreous, and possibly in early diabetic cataract.

The Adrenal Gland.—**Epinephrine,** the extract of the adrenal medulla is, as is well known, of great value as a local vasoconstrictor in ophthalmic operations. Its effect upon smooth muscle innervated by the sympathetic nervous system explains its *mydriatic effect* through stimulation of the dilator iridis. (See page 54.)

The effect of epinephrine on the intraocular tension is discussed on page 301. No ophthalmic diseases are known to result from deficiency of the adrenal medulla.

Cortin, the extract of adrenal cortex, is mentioned here because of certain enthusiastic claims of its value in glaucoma and myopia. These claims have *not been confirmed* by several reliable investigators, and there is no evidence that a deficiency of the adrenal cortex is characteristic of these or other common ocular diseases. Cortin is of life-saving value in Addison's disease in which a definite deficiency of the adrenals is at fault.

Pituitary Gland. Posterior Lobe Extract.—This substance is known to *stimulate smooth muscle*, especially of the pregnant uterus, but also other smooth muscle such as that of the blood-vessels and iris. It has been employed in glaucoma by Samojloff and others and apparently lowers the tension when 0.3 to 0.5 cc. is injected subconjunctivally. It has not, apparently, been very widely employed for this purpose. Sidlick reported that the pain of herpes zoster was greatly relieved by pituitrin. (See page 211.)

Anterior Lobe Extract.—The anterior lobe of the pituitary has been the subject of much study and a number of active hormones have been isolated, many of them having to do with regulation of the other endocrine glands. One of these, the so-called thyrotropic hormone, has been shown by Smelser to be responsible for exophthalmos in thyroidectomized animals and probably in cases of human thyroid disease. There is no definite indication for the use of these hormones in ophthalmic diseases, although the value of anterior lobe extract in the Frohlich syndrome may be mentioned. Experimental work indicates a relationship between the anterior lobe and the migration of pigment in the retina of some lower animals.

Estrogenic Substances.—Potent extracts of these substances are obtained from the urine of pregnant animals, but synthetic preparations with the same effect are now available.

The chief interest of the ophthalmologist in them is because of the cases of *headache* referred to him which do not respond to refractive correction. A certain group of these cases in women with menstrual or menopausal disturbances will obtain relief by use of estrogenic extracts in sufficient dosage. 10,000 international units of theelin or progynon weekly by intramuscular injection is sufficient in many cases.

The author has found similar treatment of apparent value in cases of *kerato-conjunctiritis sicca* in women undergoing the menopause. A number of authors have advocated estrogenic extracts in retinitis pigmentosa. The evidence for such treatment is considered on page 394.

Androgenic Hormones.—Although now available in potent form, no definite indications are known for the use of these substances in ophthalmic disease. Some work of Siegrist was based on the attractive idea that cataract, as well as other signs of senility, might be delayed or prevented by supplementing the secretion of aging sex glands. It has been shown, however, that the preparation employed was practically devoid of active hormone.

Another tissue extract, chondroitin, prepared from animal cartilage, has been investigated by Crandall, and is of interest to ophthalmologists because *its administration is attended in a respectable proportion of cases with relief from migraine* with its accompanying symptom of scintillating scotoma. Crandall has explained this as due to a detoxifying effect on some substance, possibly arising in the intestinal tract, which is normally detoxified by the liver. This detoxifying mechanism is assumed to be faulty in the subjects of migraine, but is replaced by one or more constituents of chondroitin. The substance is marketed as chondroitin sulphuric acid in 7½ grain capsules: 3 grams or 12 capsules a day should be given for a long enough period to learn whether relief will be obtained. If complete freedom from attacks occurs on this dosage, it is cut down to the amount which will maintain this freedom. In a few cases, after a considerable time, it may

be discontinued entirely. Crandall has found that about one-half the typical cases obtain relief on this regimen. Use of chondroitin is attended with no undesirable by-effects. Softening of the stools occurs in about one-half the cases, but this is seldom marked enough to cause inconvenience Patients who have very rare attacks seldom wish to undertake this form of treatment, but the author has seen a number of patients subject to frequent typical attacks who have been relieved partially or completely so long as the drug was continued.

VITAMINS AND ACCESSORY FOOD FACTORS.

Isolation of a number of vitamins in crystalline form, recognition of various clinical pictures due to deficiency of these vitamins and standardization of dosage in treating these conditions constitutes perhaps the most important advance in medicine during the past five years. Some of the more important applications of this work to ophthalmic therapeutics will be discussed.

Vitamin A.—The best known ocular disease due to a vitamin deficiency is *keratomalacia.* This condition, a true nutritional necrosis of the corneas, is seen chiefly in countries, such as China, where diet is maintained close to the subsistence level and in other countries during times of famine. It also occurs in persons with severe enteritis or acute infectious diseases in which proper dietary factors cannot be ingested or absorbed. It is associated, in early stages, with *xerophthalmia* and *night blindness,* and in many cases the condition never passes beyond the stage in which these two symptoms alone are present. Slighter degrees of deficiency occur more frequently, not only in the poorer classes, but also in persons who consider their diet normal. Certain reports of widespread vitamin A deficiency based on studies of dark-adaptation have been to some extent discounted by later observations with more accurate methods and the symptom of night-blindness is rarely noted by patients with

slight deficiencies. Other signs, however, such as atrophic changes of the skin, hair, lacrimal glands and corneal epithelium are suggestive of vitamin A deficiency. Accurate tests of dark adaptation may be of value in confirming this diagnosis. Estimation of vitamin A in the blood by the method of May is now practicable in many laboratories. Although the amount, as shown by this method, varies greatly, its results are sufficiently accurate to determine whether a marked deficiency exists and whether the dosage prescribed is sufficient to correct this. Blood determinations have not been performed in most of the cases in which a deficiency is suspected. In spite of the absence of such definite evidence, there is presumptive evidence that vitamin A deficiency plays a part in certain ocular conditions other than typical keratomalacia. Kerato-conjunctivitis sicca* due to atrophy of the lacrimal glands is one of these, as is the *mild form of epithelial dystrophy*. (See pages 263 and 264.) *Recurrent catarrhal ulcer* may be such a condition. In any form of keratitis which does not respond to the usual treatment the possibility will occur to most ophthalmologists that a deficiency of vitamin A exists and in many such cases it will be administered to remove this possibility. Cordes and Harrington have recently reported on vitamin A deficiency as a cause of intractable asthenopia associated with photophobia. Their opinion as to a deficiency was made on the basis of dark-adaptation tests and relief of symptoms when large doses (30,000 to 40,000 units a day) of vitamin A were given. Conflicting opinions are expressed regarding the value of tests with the instrument which was employed by these authors and it seems possible that the benefits observed were due to the general feeling of well-being which is noted by some persons when taking vitamin A. Some reports have appeared advocating the *local* use of vitamin A in various corneal conditions. de Roetth has shown, however,

* In a group of such cases recently studied by Puntenney no definite deficiency in the blood could be determined by May's method.

that in animals with keratomalacia the use of the oily vehicle without vitamin A was equally effective. From what we know of the function of vitamin A, there seems to be no reason to expect any effect from its local use.

Administration of vitamin A may be by the diet; milk, butter, eggs, carrots, fish and liver being especially good sources. The amount present in various preparations, with the amount necessary to supply a daily amount of approximately 30,000 units (U.S.P. or International) is given below.* Such an amount is much larger than the daily optimum for a normal adult, and is enough to supply a moderate deficiency. Larger doses may be given without undesirable effects and are often advisable in the early treatment of deficiencies. When relief of deficiency symptoms has been obtained considerably smaller doses may be continued for long periods.

Cod-liver oil—600 units per gram—dose 50 cc.
Carotene-in-oil (Pro-vitamin A)—7500 units per gram—dose 4 cc.
Halibut-liver oil—44,800 units per gram—dose 12 m.
Vitamin A concentrate—25,000 units per capsule—dose 1 capsule.

Cod-liver oil contains viosterol and the other preparations are also furnished with viosterol if desired. When the effect of vitamin A alone is desired it is best to use a preparation containing this vitamin alone, as viosterol in large amounts may have undesirable effects.

While most persons absorb vitamin A satisfactorily by the oral route, the presence of diarrhea, liver disease or vomiting and probably of an idiosyncrasy in certain persons may make *administration by the parenteral method necessary*. Thus Goldberg and Schlivek report a case with severe enteritis and kerato malacia in which the blood level remained low although 200,000 units a day were being taken by mouth. Intra-

* The error of converting grams to cubic centimeters as applied to dosage is rather small.

muscular injection of 100,000 units a day was followed by prompt healing of the corneas.

Material suitable for parenteral use is not as yet commercially available, but several manufacturers have prepared ampules containing 100,000 units in sesame oil for intramuscular injection which can be obtained for special cases or for experimental purposes.

Vitamin B Group.

Since the work of Eijkman (1897) and Funk (1911), it has been known that certain water-soluble substances present in yeast and whole grain were necessary for the prevention of polyneuritis in fowls and beri-beri in man and also for the normal growth of animals. This group of substances, originally designated as vitamin B, has been broken down into at least seven chemical compounds which may be grouped together as the *vitamin B complex.* At least three of these compounds are known to be the principal factor in preventing distinct deficiency diseases in man and knowledge is accumulating with respect to other members of the group.

Thiamine Chloride (Vitamin B_1), a thermo-labile compound, is recognized as the *antineuritic vitamin.* According to Veasey it acts as a catalyst in carbohydrate metabolism. In its absence the splitting of carbohydrates stops with the formation of pyruvic acid, a substance having a toxic effect on nerve tissue. This would explain the frequent occurrence of multiple neuritis in alcoholics who, aside from their common dietary deficiency, obtain a large part of their caloric intake in the form of carbohydrates or alcohol. Increased carbohydrate consumption creates the need for more than the average quota of thiamine. It has been shown that the multiple neuritis of alcoholics is relieved by adequate amounts of thiamine chloride, without abstinence from alcohol. Carroll and Johnson have shown that the *toxic amblyopia* of alcoholics behaves in every respect like multiple neuritis,

yielding to adequate amounts of thiamine chloride, even when the previous consumption of alcobol is continued. Restoration of normal vision was rapid in early cases, while in later cases it occurred more slowly and was often incomplete After saturating the patients with thiamine by oral dosage or by intramuscular injections, fairly large doses were continued for long periods. Since it seemed possible that other fractions of the vitamin B complex might be of value in protection or restoration of damaged nervous tissue, they advocated use of B complex in addition to crystalline thiamine chloride. (See page 332.)

The very definite results in toxic amblyopia have stimulated the use of thiamine chloride in *other forms of optic neuritis* of both the typical and retrobulbar forms. This treatment is given in addition to any other treatment indicated by the supposed cause of the disease. While the evidence in these forms of optic neuritis is by no means so conclusive as in cases of toxic amblyopia, due to the tendency of optic neuritis to improve spontaneously, there seems to be no contraindication to employing thiamine chloride in all cases, since a deficiency may be a factor in certain cases and an extra supply of the vitamin may be of value in restoration of nerve tissue when damaged by various agents. There is even some evidence that the lesions of multiple sclerosis recover more quickly with less likelihood of recurrence when large doses of thiamine chloride are provided. (See page 329.)

Especially rich sources of thiamine chloride in the food are *yeast, malt, eggs, nuts* and *whole grain*. In *pure form*, the dose of thiamine chloride is estimated either in milligrams or International units, 1 mg. being equal to 300 International units. In the conditions described above, 20 to 50 mg. (6000 to 15,000 units) is advised to be given daily by intravenous or intramuscular injection during the first week, when the dose may be cut to 10 mg. a day by injection or considerably larger amounts by mouth, as absorption by

this route is incomplete. Oral dosage should be continued for long periods in amounts of 10 to 15 mg. per day.*

The following are some of the forms in which thiamine chloride is dispensed:

Tablets of 3 mg.: 1 tablet equals 1000 International units.
Ampules 5 cc. equals 250 mg. (1 cc. equals 50 mg. or 16,666 units)
Ampules 10 cc equals 100 mg. (1 cc. equals 3000 units).

Riboflavin. Vitamin G. Vitamin B_2.

Deficiency of this fraction of the original B-complex, a thermo-stable compound, has been shown by Johnson and Eckhardt to cause a *peculiar keratitis associated with vascularization of the cornea.* In man the condition known as *rosacea keratitis*, which resembles the experimental condition, was found to clear up rapidly on adequate dosage of riboflavin. They advise saturating the patient by giving 1 mg. by vein twice a day for two to three days and then continuing with 3 to 5 mg. by mouth, either in pure form or in vitamin B complex. Sydenstricker and associates have described keratitis with vascularization of the cornea, congestion of the sclera and photophobia as part of a dietary deficiency associated with a peculiar thickening of the lips known as cheilosis. It cleared up on 3 to 5 mg. of riboflavin daily by mouth. It was only natural that this vitamin should be tried in other forms of keratitis including interstitial keratitis. There seems to be no evidence that it is of benefit in the latter condition, however, and its chief indication would seem to be in keratitis and episcleritis of the type seen in cases of acne rosacea, even though skin lesions of acne may be minimal or even absent at the time of the keratitis. The author has seen good results in a small number of such cases, though in two especially severe cases results were not definite. Results in a few cases of obstinate phlyctenulosis have been encouraging.

* Since methods for estimating thiamine in the urine and blood are available it has been found that intravenous and intramuscular doses are eliminated very rapidly. Hence Gordon and Sevringhaus advise against giving it by injection and prefer oral administration of 10 to 25 mg. per day, which should always be divided into three doses.

Since Day, O'Brien and others described the occurrence of cataract in animals on a riboflavin deficient diet, it was natural that attempts should be made to influence the course of senile cataract by the use of this vitamin. Very minute amounts were sufficient to prevent cataract in animals, and no evidence has been presented that a riboflavin deficiency is common in patients with senile cataract. There can be no objection, however, to advising patients of a possible delay in cataract formation through insuring an ample supply of riboflavin in the diet.*

Food sources especially rich in riboflavin are: liver, eggs, milk, meat, turnips and peas. In pure form it is available in ampules for intravenous injection and in 1 to 5 mg. tablets. Injections must be made by vein on account of local irritation when other routes are employed. When treating rosacea keratitis, results cannot be expected unless 3 to 5 mg. a day are employed, best after several days of intravenous injections. Some patients with little or no free HCl in the gastric secretion do not absorb riboflavin by mouth and in such cases intravenous injections must be continued for some time.

The Other Factors in the B Complex may be briefly discussed. There are at least five of these, of which nicotinic acid, B_6, and pantothenic acid are probably the most important. Nicotinic acid is the antipellagra factor, while B_6 and pantothenic acid are factors in preventing types of dermatitis in animals. In most of the conditions in which thiamine chloride and riboflavin are indicated, it seems possible that some of these factors may be of value and hence some preparation of vitamin B complex containing most or all of these factors is usually advised to supplement thiamine chloride and riboflavin.

A number of preparations are available containing varying

* According to Johnson recurrent chalazia in patients with acne rosacea respond favorably to riboflavin administration. Estimation of riboflavin in the urine is not very satisfactory, since the amounts found vary greatly according to whether the substance is being utilized properly. Large amounts may be present in the urine of patients who are not properly utilizing their supply

amounts of the factors. One preparation contains in each capsule the following factors:

Thiamin chloride. 2 mg. (666 International units).
Riboflavin: 0.5 mg. (175 Sherman units).
Nicotinamide. 10 mg.
B_6 0.25 mg.

A liquid preparation contains in each 4 cc. the following:

Thiamine chloride: 1 mg.
Riboflavin 0.83 mg.
Nicotinic acid: 5 mg
B_6 0.4 mg
Pantothenic acid. 1.05 mg.

Ascorbic Acid. Cevitamic Acid. Vitamin C.

The anti-scorbutic vitamin is of interest to ophthalmologists because of the possibility that hemorrhages in the eye might result from a deficiency and might be prevented by an adequate supply. In a number of clinics patients are saturated with ascorbic acid before intraocular operations and the incidence of postoperative hemorrhage seems to have been reduced (Urbanek). Friedenwald reported that patients with *diabetic retinopathy* showed increased capillary fragility as shown by the appearance of petechial hemorrhages in the skin after suction was applied. He considered as pathological cases showing hemorrhages after suction of less than 150 mm. of mercury and found that in such cases the fragility returned to normal limits when ascorbic acid and vitamin B complex were given in adequate amounts. Patients with diabetic retinopathy in his first series responded to treatment by freedom from recurrent retinal hemorrhages and the absorptions of older ones. Later results varied, however, and evidence arose which cast some doubt on the relationship of vitamins to capillary fragility in diabetes.* The question is still open, and it would seem logical to be sure that diabetic patients are receiving adequate amounts of ascorbic acid and B complex.

Since ascorbic acid is known to play an active part in the metabolism of the crystalline lens, Judkin and others have advised that adequate amounts be given to patients with

* Personal communications.

senile cataract. There is possibly as much reason for following this advice as in the case of riboflavin

The best food source of ascorbic acid is lemon, grapefruit and orange juice, which contain 300 to 350 International units per ounce. Twenty-six milligrams of ascorbic acid or 520 International units is considered a normal maintenance ration, and this is supplied by about 2 ounces of fruit juices Pure ascorbic acid is supplied in 25 and 50 mg. tablets. When treating patients in whom a deficiency is suspected, it is well to give 100 mg. a day for several days and 50 mg. a day for longer periods. Ampules are available for injection but absorption by mouth is usually satisfactory.

Vitamin P. Citrin.—The reports just discussed were based on the idea that the capillary fragility factor is contained in ascorbic acid. More recent work has cast considerable doubt on this assumption. While there is no doubt that certain fruit juices do contain the factor, Szent-Györgi and others believe that it is absent from pure synthetic cevitamic acid and that another factor, known as *citrin* or *vitamin P* is the anti-fragility factor. This is a glucoside isolated in pure form from hesperidin and eryodictyon but also present in paprika and fruit juices. The pure form is available chiefly for experimental purposes. Forty milligrams a day by mouth is recommended for therapeutic use. More definite information will no doubt soon be available but in the meantime it seems logical, in cases suspected of increased capillary fragility, to supply the desired amount of ascorbic acid in the form of fruit juices, which may be assumed to contain vitamin P as well.

Vitamin K.—This factor, which also has to do with preventing hemorrhage, is effective only in cases with a marked increase in prothrombin clotting time. This is present almost exclusively in cases of liver damage with jaundice and in certain cases of hemorrhage in the new-born. Hence it only rarely requires consideration by the ophthalmologist.

Vitamin D. Viosterol.—Deficiency of the antirachitic factor alone is not known to cause any diseases of the eye, with

the possible exception of lamellar cataract which perhaps occurs more frequently in children who have had rickets. Recent claims that progressive myopia is affected by viosterol seem to be without satisfactory evidence. (See page 398.) When the blood calcium is low in parathyroid tetany with cataract, normal blood calcium levels are restored more rapidly when viosterol and calcium are given with parathyroid hormone. In conditions associated with general malnutrition and lack of sunlight, such as phlyctenulosis, viosterol is usually given along with vitamin A in the form of cod-liver oil. Viosterol is the only vitamin which causes serious harmful effects when given in excessive doses. Its effect on calcium and phosphorus metabolism has resulted in abnormal deposits of calcium with hypercalcemia in some cases and hence the amounts given should be limited. The daily dose advised for the prevention of rickets in children is 10 drops of irradiated ergosterol in oil. The dose in deficiencies should be 20 to 30 drops or somewhat greater. The standardized preparations have a potency 100 times that of a good cod-liver oil, so that 2 drops of viosterol equals 1 teaspoonful of the oil. On account of the undesirable effects of viosterol in excessive amounts, the combination of vitamin A with viosterol is not advisable in the treatment of supposed vitamin A deficiency.

No definite indications are as yet known for the use of vitamin E or other vitamins in the treatment of ophthalmic disease. Vitamin E, the antisterility vitamin, in combination with other vitamins has been employed in *pemphigus* but its value is not known. Its use in *allergic conditions* in the form of large doses of wheat germ oil is in the experimental stage. In *amyotrophic lateral sclerosis* its effect has been apparently striking in a limited number of cases.

ASTRINGENTS AND LOCAL ANTISEPTICS.

This group of drugs includes *most of the metallic salts, especially those of zinc, copper, silver and mercury.* The limits to the effect produced by each of them is that of the

tolerance of the cornea and conjunctiva, and it may be said that equal effects, except in certain conditions, may probably be produced by suitable concentrations of each. These special conditions are discussed in Chapter VII. The concentrations which are safe for instillation by the patient, and which are not so painful as to require previous anesthesia, are: Mercury bichloride, 1 to 5000; mercury oxycyanide and mercury cyanide, 1 to 1500; zinc sulphate, 0.4 per cent, zinc chloride, 0.2 per cent; copper sulphate, 0.2 to 0.4 per cent. In the form of ointment at least twice this concentration is permissible, as the active agents are freed more slowly from such preparations. Silver nitrate may be used in 0.2 to 0.4 per cent solution, but the silver protein compounds, such as argyrol, neosilvol and protargol, are usually preferred for this purpose. *Their bactericidal effect is very slight, and it is probable that their astringent effect is as well secured by the zinc salts which are free from the danger of staining the conjunctiva and cornea.* This property of producing argyrosis, common to all the silver preparations, must be remembered, and should prohibit the prescription of these drugs in chronic conjunctivitis where they are likely to be used for long periods. The use of copper sulphate over long periods has been shown to produce a staining of the deeper layers of the cornea, but this has only occurred when rather strong solutions or the copper sulphate crystal have been used and for much longer periods than those which, in certain cases, have produced argyrosis. Where the organic silver compounds are used for short periods 10 per cent argyrol or neosilvol and 2 per cent protargol are suitable for use by the patient. For the treatment of localized argyrosis, see Chapter VII.

For office treatments, preceded by local anesthesia, 2 per cent zinc chloride, 2 per cent silver nitrate and 5 per cent copper sulphate solutions may be used. Any of these solutions may be dropped on the everted lids, or applied with an applicator, the cornea being protected by the lids, and the solution being washed off with normal saline immediately after the application.

Besides the metallic salts and silver compounds, a number of compounds involving the benzene ring or its derivatives have recently appeared with claims of high bactericidal power associated with relatively slight effect on the tissues. Some of these are *mercurochrome, metaphen, hexyl-resorcin, acriflavine and proflavine.* Some of the properties of these drugs are discussed in Chapter VII, as they are used in conjunctival affections. One per cent mercurochrome, 1 to 2500 metaphen, 1 to 2500 hexyl-resorcin and 1 to 1500 acriflavine may be used freely in the conjunctival sac without previous anesthesia. Solutions of two or three times this strength do not damage the cornea, and may be used after 1 or 2 drops of 2 per cent cocaine. Solutions of these drugs in alcohol-acetone are preferred by some surgeons to tincture of iodine for sterilization of the skin before operations. The stain of mercurochrome is removable only with acid alcohol, while that of metaphen may be removed with soap and water. Tincture of iodine, when used on the lids before operation, should be diluted to half strength. Tincture of metaphen, as prepared by the manufacturers, is 1 to 200 metaphen in 10 per cent acetone and 50 per cent alcohol, and may be used on the lids as such.

The fact that sensitization to these mercury derivatives occurs must be remembered. The author has seen several cases in which applications of metaphen, mercurochrome and even 2 per cent mercuric oxide ointment was followed by severe dermatitis and conjunctivitis.

An interesting comparison of local antiseptics with respect to their bactericidal power under various conditions, as well as their undesirable effects on leucocytic activity, lysozyme effect of the tears and natural bacteriolytic power of the blood has been made by Thompson, Isaacs and Khorazo. The disinfectant which showed the most rapid bactericidal effect on Staphylococcus aureus was a proprietary preparation containing alkyl-dimethyl-benzyl *ammonium* chlorides derived from cocoanut oil, now known as zephiran. It was non-irritating in 0.04 concentration but its effect was

somewhat offset by its rather marked inhibiting effect on leucocytes and lysozyme activity. Acriflavine in 0.05 per cent concentration was a fairly effective bactericide while its adverse effects on the defense mechanisms studied was much less than that of zephiran. Other interesting details as to the action of the antiseptics studied are included in their paper.

Optochin or *ethyl hydrocuprein*, the quinine derivative synthesized by Morgenroth, *is useful in pneumococcic conjunctivitis and keratitis.* The hydrochloride is employed in solutions, the base being soluble only in oils. Solutions must be freshly made up for each case. A 1 per cent solution may usually be employed by the patient, but certain patients complain of pain after its use. A difference in this respect with solutions from various sources has been noted, so that it is best to try each solution in the office and when necessary a weak local anesthetic may be given to be instilled before the optochin. The temporary pain caused by optochin is followed by relative anesthesia persisting for an hour or longer.

DRUGS PRODUCING LOCAL VASODILATATION.

The most important drug used for this purpose is dionin (ethyl morphine). Instillation of this in 1 to 10 per cent solution *produces a marked dilatation of the conjunctival vessels and chemosis of the conjunctiva.* Various therapeutic powers have been ascribed to dionin, which is used by many ophthalmologists in all types of ocular inflammation. Probably all its effects are to be ascribed to vasodilatation, with resulting improvement in the nutrition of the cornea and sclera and an increase in the antibodies reaching these tissues from the blood stream. It has been demonstrated that other drugs, such as atropine, are more readily absorbed after dionin has been given; hence it is often employed in iritis and keratitis accompanied by iritis. Following the slight initial pain after instillation a relative analgesia occurs, lasting one hour or longer, which is another reason for its

use. The effect of this increase in the lymph supplied to the cornea is said to aid the absorption of fresh corneal scars, and it is probably well to advise its use for several months after a corneal ulcer for this purpose. Patients vary in their reaction to dionin, and it is well to try the effect of 1 drop on each patient in the office before prescribing the drug for home use. If the reaction to the 5 per cent solution is unusually marked, a 1 or 2 per cent solution is prescribed at first, the strength being increased later as a tolerance to the drug develops and the reaction becomes less intense. Otherwise a 5 per cent solution in 1 to 1500 mercuric cyanide is usually given with instructions to increase the number of drops used as the reaction subsides.

In corneal ulcers, where an especially intense reaction is desired, a few grains of dionin powder may be dusted on the ulcer, or 3 to 8 minims of 5 per cent solution may be injected subconjunctivally in the region of the ulcer. Here the presence of mercuric cyanide, usually 1 to 3000, is considered by some authors as the important factor in the effect on active keratitis, the dionin acting to lessen the pain of injection. In any case, the effect of dionin on this pain, which is otherwise severe, is very definite, and with it no pain is usually felt after the first few seconds. Such injections have been used in cases of threatened panophthalmitis after a wound or of beginning infection after cataract operation, and though their effect may be questioned, a trial is justified in such desperate conditions. The author has seen apparently definite effects in some cases of corneal ulcer which had resisted other forms of treatment.

In *epithelial dystrophy of the mild type* a definite effect both on the symptoms of irritation and on the appearance of the corneal epithelium may usually be observed, and for this purpose a 5 per cent solution is usually prescribed for use three or four times a day. The use of dionin in incipient cataract, doubtful as are its effects, is described in Chapter X.

It must be remembered that dionin is an opium derivative, and that systemic symptoms resembling those of morphine

are produced by large subconjunctival injections of 5 per cent solution. Hence an amount of 10 minims should seldom be exceeded and considerably less than this must be the maximum in children. The drug comes under the provisions of the law regulating narcotics, so that prescriptions must be renewed by the physician himself and must be written to comply with the law.

The use of *yellow oxide of mercury ointment* for massage of the cornea and lids probably rests upon the vasodilatation produced. It acts as a lubricant, allowing the cornea to be massaged through the lids, and probably also as a mild local irritant, and hence is of equal value with dionin in early corneal scars. Its bactericidal effect may also play a part where it is employed in cases of chronic conjunctivitis or phlyctenulosis.

Jequiritol was formerly much used to aid in absorbing corneal scars, especially those due to trachomatous pannus, by the severe local inflammation produced. This inflammation sometimes produced serious effects, however, so the treatment is not now much employed. Roemer showed that by making graduated solutions of its active principle, abrin, in glycerin, reactions of any degree might be produced, and it is probable that such preparations might be used with advantage as a substitute for dionin in certain conditions. Interesting observations were made on local immunity with abrin, and a serum was produced which would check or prevent entirely the inflammation resulting from its use. In any case, the drug must be used with caution, especially by those unfamiliar with its effect.

DRUGS PRODUCING GENERAL VASODILATATION.

The effect of these drugs is desired chiefly in vascular conditions affecting the retina and optic nerve which are not easily accessible to local treatment. This is especially true in *closure of the central artery* or its branches. (See Chapter XII.) The most rapidly acting drug is amyl nitrite which produces instantaneous flushing of the face when 3

minims are inhaled. *Nitroglycerine* (dose $\frac{1}{100}$ grain by mouth) acts less promptly while *sodium nitrite* produces an even slower, but more prolonged effect. It may be given in doses of 1 or 2 grains three times a day. Perhaps the most marked effect of the nitrites is that following intravenous injection of 1 cc. of 10 per cent sodium nitrite, as recommended by Duggau. *Erythrol tetranitrate* (dose $\frac{1}{2}$ grain) is said to produce a more prolonged effect than that of sodium nitrite.

Acetyl-cholin is claimed by French authors to be a more powerful vasodilator than the nitrites, affecting especially the smaller arterioles and capillaries. 0.1 to 0.3 gram is given subcutaneously daily or every two days. (See Chapter XII.)

A drug of an entirely different group has recently been advocated by deTakats and others for the relief of arterial spasm. This is *papaverine,* an opium derivative, which is given in emergencies by vein in $\frac{1}{2}$ grain doses. It may also be given by mouth in doses of 1 grain. According to deTakats, the drug is safe when given in this dosage and is more effective than other vasodilators.

Recent work by Lambert, which casts doubt on the efficacy of all drugs which lower the general blood-pressure, will be discussed later.

The advantages of heat in producing or maintaining vasodilatation during administration of other drugs should not be forgotten.

DRUGS CAUSING VASOCONSTRICTION.

Epinephrin Chloride in 1 to 1000 solution produces marked constriction of the conjunctival vessels. Such instillations produce a very unpleasant sensation of muscular spasm, and should be preceded by cocaine or butyn. When prescribed for home use, as in vernal conjunctivitis, a 1 to 4000 solution with the addition of 40 grains of boracic acid to the ounce is well tolerated. *Ephedrine* in 3 per cent solution produces a similar local effect, but its effect on the pupil is more marked, which may be undesirable.

The synthetic derivatives of epinephrine produce similar

effects on the vessels in suitable concentration, but in such concentration the mydriasis produced may offer inconveniences. The use of neosynephrine in angioneurotic edema of the lids and conjunctiva has been described (page 58).

DRUGS EMPLOYED TO PREVENT OR CONTROL HEMORRHAGE.

Hemorrhage occurring in operations on the lids, orbit or lacrimal sac is occasionally persistent enough to call for special consideration. Even more important is the occurrence *of intraocular hemorrhage, especially following operations* for cataract, retinal detachment, or glaucoma. If the patient's coagulation-time is known to be low, if a general condition such as anemia is present which might predispose to hemorrhage, or if hemorrhage has occurred at a previous operation, measures to prevent its occurrence will be considered.

The administration of calcium by mouth for several days before operation is the measure most commonly employed, 15 to 30 grains of calcium lactate being given by mouth t.i.d. Deficiency of blood calcium is exceedingly rare, however, and most pharmacologists doubt if this procedure affects the coagulation-time in any way unless such a deficiency exists.

Attempts have been made to supply another important factor in coagulation, the thromboplastic substance which acts on prothrombin in the presence of calcium to convert it into fibrin. Substances prepared from brain (cephalin), and lung tissue have been shown to hasten coagulation *in vitro* and when applied locally to wounded tissues. Suspensions of such material dispensed as Fibrogen, Thromboplastin and Cephalin are probably useful when applied in full strength to bleeding areas. They have been given subcutaneously and even orally but it is doubtful if any effect can be expected from such medication, and hence these preparations do not answer our need in the control of intraocular hemorrhage.

Such hemorrhages apparently depend on local conditions in the blood-vessels which are not amenable to medication, or on an increase in general blood-pressure. The practice of bleeding patients with high blood-pressure before operation, which is practised in some clinics, is not likely to prevent hemorrhages, since a compensatory rise of blood-pressure occurs almost immediately. Rest in bed and general measures to reduce blood-pressure before operation are apparently of more value than any of these procedures. Elevation of the head of the bed to prevent congestion of the head and the use of cold postoperatively may lessen the tendency to hemorrhage.

In conditions associated with increased capillary fragility, such as diabetes, the use of fruit juices in large amounts, containing vitamins C and P, or of concentrates of these vitamins, may be important. The rationale of such treatment is discussed on pages 84 and 85, as is the use of vitamin K to prevent hemorrhage in cases with prolonged prothrombin clotting time.

DRUGS USED BY THE SYSTEMIC ROUTE AGAINST INFECTION.

Remedies Against Syphilis.—Remedies against syphilis are of great importance in treating the ocular manifestations of that disease. In general, the same rules which govern therapy in other forms of syphilis will apply in these ocular conditions. There are only a few special applications of these rules which are particularly important to the ophthalmologist. Syphilis affecting the eye involves a relatively small organ, where a small amount of damage may produce disastrous permanent effects on the visual function. Hence there is *special need for early diagnosis and the immediate institution of vigorous measures.* The author differs with many syphilologists who advocate beginning with very small doses of the arsenicals, usually after a preparatory course of mercury or bismuth, for fear of bringing about a Herxheimer reaction. He has so often seen severe damage to the eye result from delay in

reaching effective dosage that he prefers in nearly all cases to begin with relatively large doses of the arsenicals, the usual precautions to avoid toxic reactions being, of course, taken. Even in optic neuritis, where some authors particularly fear the Herxheimer reaction, he has never had cause to regret this course. If the ophthalmologist prefers to refer his cases to a syphilologist he should insist on the importance of losing no time in giving effective doses of active therapeutic agents. Local treatment, such as the use of atropine in iritis and keratitis, should not be neglected because of one's faith in specific therapy, and cases referred elsewhere for systemic treatment should be kept under constant observation by the ophthalmologist. The special conditions present in interstitial keratitis, where the other eye may become affected in spite of treatment, but where active treatment is none the less important, and in tabetic atrophy, where ordinary systemic treatment is powerless and special measures are required, are discussed in Chapters VIII and XIII. The future of the patient whose ocular symptoms have been relieved, but whose syphilis remains uncured, must, of course, be remembered, and if the ophthalmologist has been conducting treatment until this time the patient should be placed in proper hands so that his treatment may be continused until all danger from syphilis is past.

The Sulfonamide Group.—Our knowledge of this group of drugs undoubtedly constitutes the most important advance in chemotherapy since Ehrlich's synthesis of salvarsan. Although sulfanilamide was first produced in 1908, this was done in the German dye industry and the bacteriostatic properties of this group of drugs was not put to any clinical use until 1933. In this year a German, Foerster, reported the first case of human infection in which the value of these drugs was demonstrated, a sulfonamide compound known as streptozon being employed. This case was one of staphylococcus infection, but it was recognized after the fundamental experimental work of Domagk in 1935, that preparations then available were especially effective against infec-

tions with virulent hemolytic streptococci. Clinical reports increased in number, appearing in France and England during 1935 and in America in 1936, when Long and Bliss and Mellon and Rosenthal began a series of experimental and clinical reports. Marshall in 1937 reported on the absorption, toxicity and other properties of the drugs, and in 1937 sulfanilamide was accepted by the Council for New and Nonofficial Remedies of the American Medical Association. The first reports on the use of the drugs in ophthalmological conditions were made in 1937 by Hageman in Germany and Heinemann in the Dutch East Indies, both of these authors reporting rapid healing in cases of gonorrheal ophthalmia. The monograph of Long and Bliss summarizes our knowledge of these drugs in 1939 and a review by Guyton in the same year covers ophthalmological contributions to that time.

At the time of Guyton's report, over one thousand compounds of this group had been prepared. The early ones, known as prontosil, neoprontosil, prontylin, streptozon, and rubiazole were combinations of sulfanilamide with azo dyes. It is now generally accepted that the active agent in these preparations was sulfanilamide and that this substance alone possesses all the advantages of its various azo-derivatives. It was found to be effective not only against streptococcic infections, but also against those due to the meningococcus, gonococcus, and certain viruses. It was moderately effective in certain pneumococcic infections, but in 1938 Whitby introduced another sulfonamide derivative, sulfapyridine, which was definitely superior in *pneumococcic* infections. It was also effective against the gonococcus and the question remains open as to whether it is superior to sulfanilamide in gonococcal infections. A third derivative, *sulfathiazole*, prepared by Lott and Bergeim in 1939, seemed to demand attention because it was more effective than the others in *staphylococcic* infections, apparently as effective as sulfapyridine in pneumococcic and gonococcic infections, and productive of fewer toxic reactions. It seems that these three derivatives, sulfanilamide, sulfapyridine and sulfathiazole, possess

all the desirable properties of the preparations so far synthesized. The relative *effectiveness* of each drug in various types of infection can only be stated in so far as present evidence warrants and, in the case of many infections, this is as yet insufficient.

The *mode of action* of these drugs has been much discussed. The opinion expressed by Long and Bliss seems to have found fairly general acceptance in principle, although certain details remain undecided. The explanation which they accept is based on the *bacteriostatic effect* of the sulfonamide group, which acts in the blood stream and tissues as it does *in vitro*. Although this effect is relatively weak as compared with that of many other antiseptics, the great diffusibility and relatively low toxicity of the drugs makes it possible to maintain a concentration in the blood and tissues great enough to prevent multiplications of certain organisms in the body until the natural defenses have been raised to a point capable of killing the organisms and disposing of their products. Evidence for and against other effects of the drug, such as stimulation of phagocytosis or other defense mechanisms are discussed by Long and Bliss, who feel that most of the known facts can be explained on the above simple theory. There is some evidence that certain toxic bacterial products are neutralized by the drugs. Acceptance of the bacteriostatic theory indicates the importance of maintaining an effective concentration of the drug in the blood and tissues until the infection is overcome, since any drop below the effective level allows the organisms to multiply and the struggle must be begun once more. Doses too small to produce such a concentration in the tissues are probably of no value whatever, and many early failures to secure good results with these drugs were undoubtedly due to insufficient dosage. Some reports of success with doses of the drugs too small to have any bacteriostatic effect seem to represent coincidental spontaneous improvements. The drugs are, of course, ineffective in conditions not due to infection and hence all reports of their effect in such conditions as glaucoma, recurrent

corneal erosion and various degenerative conditions may be disregarded.

Failure to secure effective dosage in early cases was due to *fear of the toxic effects of these drugs.* There is no doubt that certain definite toxic properties are common to all members of the group and that their effects may be exceptionally severe when the drugs are administered to especially susceptible persons. By observing certain precautions, however, it is possible to give the drugs in effective dosage with very few serious or alarming reactions. Patients taking any of the sulfonamides should be at rest and should be seen every day by the physician. A blood count and hemoglobin determination should be made every second day. When the larger doses are being given patients should, if possible, be hospitalized and the blood level of the drug estimated frequently during the first few days of most intensive treatment. A history of previous use of the drugs, with any undue reactions observed, should be taken in every case, as history of a previous severe reaction indicates extreme caution in use of the same drug and usually any other member of the group. An adequate amount of fluid should be taken, 3500 cc. for an adult, but this should not be exceeded, as otherwise it is difficult to maintain a proper blood level of the drug.

A certain amount of nausea and anorexia is common when any of the drugs are being taken by mouth. This is not a serious inconvenience, however, unless vomiting prevents proper dosage. In this case medication may be given by enema or parenterally. Headache and tinnitus are not uncommon symptoms but are of no serious importance. Cyanosis is commonly observed with sulfanilamide, less commonly with sulfapyridine and sulfathiazole. It is due to a colored substance, as yet unknown, formed in the blood stream by the drugs. As a rule it is not of serious importance and unless accompanied by marked changes in the blood picture is no indication for stopping the drug. Dyspnea is noted chiefly in ambulatory cases and is an indication for less physical exertion. Gastric intolerance is more com-

monly severe with sulfapyridine, and the occurrence of various skin rashes is more common with both sulfapyridine and sulfathiazole than with sulfanilamide. Sulfapyridine has the peculiar property of being precipitated in the kidney tubules and ureters, occasionally causing serious obstruction, when it must be discontinued. Acidosis occurs only with sulfanilamide and hence sodium bicarbonate is usually given in one-half the amount of the drug. Alkalies are not necessary when the other drugs are given.*

Reactions which call for immediate discontinuance of the drug are *acute hemolytic anemia, agranulocytosis, dermatitis* of the *exfoliating type, hepatitis* and, as a rule, *fever*. A moderate gradually developing anemia is not uncommon and does not call for discontinuing the drug unless the hemoglobin drops below 60 per cent. Rapidly developing hemolytic anemia is rare but may be serious and it is because of this possibility that the blood picture must be watched. Agranulocytosis is very rare, the usual drop in white count to normal resulting from control of the infection. Fever occurs in from 9 to 15 per cent of patients, and is about equally common with all three drugs. According to Long and Bliss, it is a warning sign of more severe complications and usually indicates stopping the drug. Such febrile reactions must be distinguished from those due to the original infection. Hepatitis is rare but may be serious. At least one case of *optic neuritis* has been reported as due to sulfanilamide, but such an occurrence must be exceedingly rare. Long and Bliss have found no clinical evidence suggesting incompatibility between the sulfonamides and other drugs or general anesthetics. Alcohol apparently increases the symptom of dizziness and should not be allowed to patients taking the drugs.

* A few cases of *transient myopia* have been reported as due to sulfanilamide. Ciliary spasm may have been the cause in some cases, while in others cycloplegics were without effect and a temporary change in refractive index of the lens, comparable to that which occurs in diabetes, has been hypothecated. A peculiar ocular reaction not infrequently seen with sulfathiazole is *hyperemia of the bulbar conjuctiva*. Neither of these reactions is important.

Sulfanilamide is the most diffusible of the three drugs. It is absorbed almost completely from the intestinal tract, more rapidly when given in solution or crushed and put into suspension in water. It penetrates practically all the tissues of the body within fifteen minutes to one-half hour after a single large oral dose, reaching its maximum in the blood within two to three hours. It is excreted rapidly, so that in order to maintain adequate blood levels oral doses must be repeated every four hours day and night. Bellows and Chinn have shown that after single large doses in dogs it could be detected in the ocular tissues and fluids within fifteen minutes and reached its maximal concentration in four to six hours. When the blood level was 19.1 mg. per 100 cc., the amounts in the various ocular tissues and fluids were as follows: aqueous, 11.6 mg.; lens, 8.6 mg.; vitreous, 8.6 mg.; corneo-scleral layer, 12.3 mg.; chorio-retinal layer, 15 mg. per 100 cc. The drug disappeared quite rapidly from the ocular tissues, small amounts only being present after forty-eight hours, except in the lens which was slowest to absorb and slowest to lose the drug. When given over several days in divided doses corresponding to those employed clinically, the amounts in the lens, corneo-scleral and chorio-retinal layers remained practically the same as those in the blood, the amounts in the aqueous and vitreous being somewhat less. Guyton found 6.9 mg. per 100 cc. in the aqueous of a patient who had been on repeated doses and whose blood level was 7.4 mg. per 100 cc. Mengel in one human eye at enucleation found 2 mg. per cent in the vitreous when the blood level was 5.1 mg. per cent, while in a second eye the amounts were 3.2 mg. per cent in the vitreous and 3.7 mg. per cent in the blood. In a third eye, thirty-two minutes after one oral dose of 20 grains, the vitreous contained 1.1 mg. per cent.

Sulfanilamide is especially effective in infections due to the *streptococcus*, *meningococcus*, *gonococcus* and *Welch bacillus*. It is hence indicated in ocular conditions presumed to be due to these organisms, including *orbital cellulitis* in erysip-

elas, *endophthalmitis* during meningitis, scarlet fever or measles, and some case of *traumatic* or *postoperative intra-ocular infection*. Guyton and others have reported cases of this type in which sulfanilamide seemed definitely responsible for saving eyes which would otherwise have been lost. One of Guyton's cases of endophthalmitis during meningococcic meningitis recovered vision of 20/20. Cases of *serpent ulcer* due to the streptococcus have responded well to the drug. It seems of probable, though less definite, value in brucellosis and pneumococcal infections. None of the sulfonamides seem to be of great value in tuberculous conditions. The evidence varies with regard to their effect in virus diseases. There seems to be no doubt, however, that sulfanilamide is of value in *trachoma* and *inclusion blenorrhea*. Guyton reviews reports covering 250 cases of trachoma treated with the drug, including the first reports in 1938 by Sie Boen Lian and Loe which will be discussed later. Thygeson in 1939 and subsequently reported disappearance of inclusions in inclusion blenorrhea within two days and clinical cures in thirteen days or less. Reports on use of the drug in gonococcal conjunctivitis have been numerous and there is no doubt that it greatly shortens the period of hospitalization and is of great value in preventing corneal complications. (See page 219.) Guyton's results in cases of *iritis* were not very encouraging, but this may have been due to the type of case available for treatment since others have reported good results in iritis due to focal infection.

Gamble and a few others have reported success in treating *sympathetic ophthalmia* with sulfanilamide, but cases have not yet been numerous enough to state definitely which of the three drugs is to be preferred or whether any of them possess definite advantages over previous methods.

The *dosage* of *sulfanilamide* will depend upon the type of infection present. In severe rapidly progressive infections which threaten loss of the eye, the chance of obtaining undesirable reactions must be risked in order to obtain the full therapeutic effect of the drug. Such conditions are endoph-

thalmitis, traumatic or postoperative intraocular infections, serpent ulcer, orbital cellulitis and very severe gonococcal conjunctivitis. In such conditions, a blood concentration of 10 to 12 mg. per 100 cc. should be obtained as quickly as possible and maintained at this point until the infection shows definite signs of subsiding. This is best done by giving a large initial dose of pulverized sulfanilamide by mouth, usually 80 grains for an adult weighing 150 pounds. For children the dose should be somewhat larger in proportion to weight. The drug is emulsified in water, and one-half to two-thirds the amount of sodium bicarbonate is given at the same time. Smaller doses sufficient to maintain the same blood level are given at four-hour intervals day and night. The following table, condensed from that of Long and Bliss, gives the dosage advised in severe infections in relation to body weight:

Weight in pounds	Initial oral dose, grains.	Maintenance oral dose q. 4 hours, grains
150	80	20
125	70	15
100	60	15
75	60	15
50	50	10
25	30	5

This amounts to a daily dose of about 1.2 grains per pound in most adults and 1.8 to 2 grains per pound in children.

How long this dosage should be continued will depend upon the response of the infection and, in some cases, upon the appearance of toxic symptoms. It may be maintained in most cases for three to five days, by which time infections which are susceptible to this treatment will usually show marked improvement. Under these conditions, the dosage may be cut to 20 grains every six hours for an adult for the next two days and then continued at 15 to 20 grains four times a day until all signs of active infection are absent. *The condition should be watched closely and if* signs of recurrent inflammation are observed, larger doses should be resumed.

In less severe infections smaller doses, sufficient to obtain a blood level of *4 to 8 mg. per 100 cc., are often sufficient.* Such conditions include acute iritis, trachoma, inclusion blennorrhea and most cases of gonococcal conjunctivitis. A table of dosage, calculated to produce the desired level in such conditions, again adapted from Long and Bliss, follows:

Weight in pounds.	Dosage per 4 hours, grains.
150	15
125	15
100	15
75	12
50	10
25	5

Such doses may be continued longer than the larger ones and, in chronic infections, 45 to 60 grains a day may be necessary for periods of several weeks or even longer.

In the rare cases in which sulfanilamide cannot be given by mouth or by nasal tube, it may be given parenterally. Long and Bliss recommend a 1 per cent solution in 1/6 molar sodium lactate or physiological salt solution. In severe infections they recommend larger doses by this route than by mouth, one-half the total first day's dose being given in the subcutaneous tissues at the first injection and one-third of this dose every eight hours thereafter.

Local use of sulfanilamide has been employed by surgeons in treating infected wounds and by a number of ophthalmologists. Rambo showed the tolerance of the tissues for a saturated solution (0.8 per cent) and of a 50 per cent suspension of the drug in olive oil both by instillation and subconjunctival injection. He was able to control experimental streptococcal infections by injecting the saturated solution into the aqueous in small amounts. Others, including Cosgrove, used the solution in treating trachoma and felt it was of value, but the cases were not followed long enough for a definite opinion. Smith, Julianelle and Gamet, using 2.5 per cent neoprontosil, saw improvement during the first week of treatment, but observed no further effect on the disease.

Spining, in gonococcal conjunctivitis, found local use of the drug ineffective while its oral administration in the same cases was later effective. Reports on penetration of the drug into the eye when applied locally have varied greatly. Bellows and Chinn, after dusting powdered sulfanilamide on the cornea, were unable to detect it in the aqueous after one hour. Mengel, after repeated instillation of 0.8 per cent solution during two hours, found only faint traces in the aqueous. Guyton, however, after instilling 0.8 per cent solution every ten minutes for four hours in the eyes of rabbits, found levels of 2.1 to 8.7 mg. per cent in the aqueous. When using a 5 per cent ointment every half hour for four hours, he found exceedingly high concentrations of the drug in the aqueous, varying from 26.9 to 39.9 mg. per cent. He considered that the amounts present in the cornea were probably even larger. The preparation which produced the smoothest and least irritating vehicle for the drug is described as follows:

"Ten parts of sulfanilamide are dissolved in 25 parts of boiling water and 4 parts of sodium alginate in 75 parts of boiling water. These are mixed and stirred until cool, the sulfanilamide and sodium alginate precipitating out in a smooth colloidal form. Sixteen parts of aquaphor, 1 part of sodium chloride dissolved in 4 parts of water, and 78 parts of white vaseline are added and the mixture stirred until a smooth creamy ointment results."

Using this ointment in cases of conjunctivitis due to the staphylococcus, Koch-Weeks bacillus, streptococcus and pneumococcus, no superiority could be determined over use of the ointment base alone. This was also true in a small group of patients with trachoma. In corneal ulcers, however, the results were encouraging as all cases, including 3 of hypopyon ulcer due to the staphylococcus, healed promptly. The ointment was used every hour day and night in these cases, and Guyton emphasizes the need for frequent applications if the desirable level in the tissues is to be maintained.

Neoprontosil in 2.5 per cent solution was investigated in

this work but no sulfanilamide was found in the aqueous after instillation and only small amounts after subconjunctival injection. This was to be expected, according to Guyton, since neoprontosil only frees sulfanilamide in the tissues and is inactive *in vitro*.

From this work it must be concluded that effective concentrations of sulfanilamide can be maintained in the aqueous and presumably in the cornea and conjunctiva only by frequently repeated applications of a concentrated ointment. Whether the results of this method are superior to those produced by adequate oral dosage has not as yet been determined.

Sulfapyridine is less uniformly absorbed from the intestinal tract than sulfanilamide and is also less diffusible. More of it is conjugated in the blood into an inactive form than is the case with sulfanilamide and this varies greatly in certain persons. Hence it is more difficult to obtain effective concentrations of this drug in the blood and tissues. Chinn and Bellows, after large single doses in dogs, have found small amounts in the aqueous and ocular tissues after fifteen to thirty minutes. The amounts reached a maximum after three to four hours. When the blood level was 6.1 mg. per 100 cc., the amounts in the ocular tissues and fluids were as follows: aqueous 5.8, vitreous 3.2, sclera 7, cornea 6.8, lens 1.1, retina 6.3 mg. per 100 cc. A property of this drug not noted with sulfanilamide is its retention for longer periods in certain ocular tissues. Thus the retina and sclera contained 11.5 mg. per 100 cc. after twelve hours, amounts considerably larger than were ever found in the blood with the dosage employed. Pinkhof in rabbits on oral dosage found that the amount in the conjunctival secretion was 50 to 100 per cent and that in the aqueous and vitreous was 25 to 33 per cent of the amount in the blood.

The drug, as has been stated, is especially effective against *pneumococcus infections*, and is probably equal to sulfanilamide in those due to the *gonococcus*. Sysi reported that negative smears were obtained in most of his cases of gono-

coccal conjunctivitis within twenty-four to forty-eight hours. A few favorable reports on its use in *trachoma* have appeared but there is not as yet evidence that it is superior to sulfanilamide in that condition or in inclusion blenorrhea. Lee and Rottenstein reported good results in 2 cases which had resisted sulfanilamide. According to Guyton, it is effective in *Koch-Weeks conjunctivitis*. In *staphylococcic* infections it is more effective than sulfanilamide but probably not so effective as sulfathiazole.*

The *dosage*, because of variable absorption, is not so easy to regulate as that of sulfanilamide, requiring more frequent blood determinations. The desirable level in most types of infection is from 4 to 6 mg. per 100 cc., higher levels being desirable in virulent intraocular infections. To obtain these levels the amounts listed in the table on page 102 for sulfanilamide must be given and must be increased if blood determinations show unsatisfactory levels. As previously stated, it is not necessary to give sodium bicarbonate with this drug.

Since 20 per cent of patients suffer from nausea and vomiting when taking sulfapyridine, it will more often be necessary to substitute one of the other derivatives. In proven pneumococcic infections in such persons, however, it may be given in 0.15 per cent solution by vein, or in the 5 per cent solution of its sodium salt. With this latter preparation, care must be taken not to inject outside the veins.

Sulfathiazole, the thiazole derivative of sulfapyridine, possesses most of its properties with certain *exceptions*. It does not so often cause urinary obstruction by precipitation in the urinary tract, and vomiting is much less common when it is employed. A peculiar reaction often noted is marked conjunctival hyperemia which is of no importance. It was noted that, on account of its slightly larger molecule, it penetrated less easily into the spinal fluid. Bellows and

* A recent report by Lepard (American Academy of Ophthalmology and Otolarygology, 1941) presents evidence that sulfapyridine is of value in *keratitis due to Bacillus Pyocyaneus* It was given in large doses systemically, but there seems reason to advise local use of sodium sulfapyridine in addition to this

Chinn have shown a great difference between this drug and the derivatives just discussed in diffusibility into the ocular tissues. When the blood level in dogs was 7.4 mg. per 100 cc., only 0.4 mg. per 100 cc. was found in the aqueous.

The sclera showed a power to retain this drug in large amounts such as was observed with sulfapyridine.

Few clinical reports have appeared on the use of sulfathiazole in ophthalmic diseases. It would seem to be the drug of choice, however, in *staphylococcic* cellulitis of the lids and orbit and in obstinate staphylococcic conjunctivitis. In *gonococcal infections* it may prove as effective as sulfapyridine with less objections on the grounds of gastric intolerance. The *slight diffusibility* of the drug into the intraocular media would seem to make it *relatively ineffective in cases of intraocular infection.**

Local Use of Sulfapyridine and Sulfathiazole.

Both of these drugs are much less soluble than sulfanilamide and hence their use in solution is impractical. The sodium salt of both drugs is quite soluble, but on account of its high alkalinity is rather irritating. Using a 4 per cent ointment of sodium sulfapyridine every half hour for four hours, Guyton found levels of 1.6 and 1.3 mg. per cent in the aqueous. Thygeson† has seen good results in staphylococcic conjunctivitis from the use of a 5 per cent ointment of sulfathiazole sodium, and considers it the most effective form of local treatment in this condition. The penetration of sulfathiazole through the cornea when applied locally has not been studied, but from the observation by Bellows and Chinn as to its penetration of the blood-aqueous barrier, it seems likely that it will prove to be low. The peculiar property of the cornea and sclera of absorbing and retaining both

* On account of the difficulty in obtaining constant blood-levels when sulfathiazole is given by mouth, Spink advises the intravenous use of sodium sulfathiazole in critical cases; 60 grains are given as an initial dose, followed by 15 grains every six hours. Since the drug is very rapidly excreted, the oral dosage necessary to maintain effective levels must, in some cases, be 1½ times the usual dose of sulfanilamide.

† Personal communication.

these drugs in large amounts from the blood stream which was observed by Bellows and Chinn has been noted. This has been confirmed by Myers and his associates for sulfapyridine.

In addition to the three drugs of the sulfonamide group previously discussed, one other may be mentioned, although it has only recently been studied. This is sulfadiazine, a drug allied to sulfapyridine. According to Plummer and Ensworth it is less toxic than sulfapyridine and sulfathiazole and is capable of producing and maintaining more effective blood levels on oral administration. It is recommended in infections due to the pneumococcus, streptococcus, staphylococcus and Friedländer's bacillus.*

The Salicylates.

Before the advent of the sulfonamide derivatives, the drug most employed in non-luetic ocular inflammation was sodium salicylate. In iridocyclitis due to focal infection the effect of large doses on pain and on the objective signs of inflammation was often dramatic and there seems no doubt that such therapy was of value in sympathetic ophthalmia. The response of such conditions to the salicylates is similar to that observed in rheumatic fever, in which relief is nearly always obtained, not only from pain and fever, but also from swelling, redness and immobility of the joints. In spite of such clinical observations, the mode of action of this group of drugs has never been satisfactorily explained. The bactericidal effect of sodium salicylate is slight. A concentration of 1 to 250 is required to produce bacteriostatic effect on most organisms *in vitro*, and such a concentration cannot be obtained in the tissues with even

* As more clinical experience with sulfadiazine has accumulated, the extreme rarity of toxic reaction has been confirmed, and its bacteriostatic effect on a variety of organisms. According to Spink, the blood level must be watched, as slow excretion offers the possibility that undesirably high blood levels may be reached. It is much more diffusible than sulfathiazole and hence might prove of crucial value in intraocular infection due to the staphylococcus or *meningococcus*. It may be given by vein in a 5 per cent solution of its sodium salt

very large therapeutic doses. Salicylic acid is a much more active antiseptic but because of the reaction of the tissues it cannot exist in free form in the body. Boots and Cullen in experimental arthritis found that the organisms employed were not affected by large doses of the salicylates, but that the inflammatory changes produced by the infection were definitely less when the drug was employed. Hanzlik, after thorough study, concluded that the effects of this group could not be explained as due to a bactericidal or bacteriostatic effect. It is known, however, that the salicylates cause an increased elimination of uric acid and possibly other products from the body and an increase in blood sugar. This results in dilution of the blood by osmosis, a mechanism which may in part explain the reduction in temperature produced by the drugs. Sollman states that the effect of the salicyl group in rheumatic fever "is probably connected with their analgesic and antipyretic action."

Sodium salicylate is well absorbed by mouth and is extremely diffusible. The author could demonstrate the salicyl radical in the aqueous of rabbits within twenty-five to forty minutes after oral dosage and after forty minutes the amount present could be estimated quantitatively. A concentration of 1 to 3500 to 1 to 1250 was reached in the aqueous of some animals and the whole eyes showed a concentration of 1 to 5000. The amounts present in the eye could be increased, according to Whitham, by local heat and applications of dionin. Sodium salicylate may be given by vein but since an equal concentration and effect may be obtained almost as rapidly by oral dosage, there is seldom any indication for intravenous injections. Since the drug is rapidly excreted in the urine, frequently repeated doses are necessary to maintain concentrations in the blood and tissues sufficient for relief of symptoms. The dose of sodium salicylate proposed by H. Gifford in 1900 was *1 grain per pound of body weight per day*. This is sufficient to obtain relief in many cases of uveitis, though in severe cases, especially of sympathetic ophthalmia, 180 to 200 grains per day

may be advisable for the first two or three days of treatment. If relief is obtained it may then be cut to 90 grains per day and, after a week, to 60 or 75 grains per day. Another method of administration is the use of 15 to 20 grains every hour until symptoms of tinnitus and nausea occur. The drug is then stopped for twelve hours, after which 15 grains is given every four hours until relief of symptoms is complete (Sollman). If vomiting occurs, a retention enema containing 90 grains may be employed. This may be repeated after twelve hours, and then at twenty-four hour intervals. The nausea is by no means entirely relieved when this method is employed, since it is partly due to the central effect of the drug. Other toxic effects include albuminuria, which is transient and need not be considered an indication for stopping the drug unless other evidence of kidney damage is present. Since there is some possibility of aggravating a preexisting nephritis, urinalysis is advised in every case before full dosage is begun. The tinnitus may be exceedingly annoying and even cause some degree of deafness, but this clears up soon after the drug is stopped. Dizziness and even mental confusion are noted by some patients, but this is seldom serious enough to justify stopping the drug. Serious toxic reactions are exceedingly rare, no symptoms even alarming having ever been observed by the author. Sodium salicylate may be given in liquid form although the taste is impossible to disguise. The following prescription containing 15 grains to the dram is a convenient one:

Sodium Salicylate	oz. i
Simple Elixir	oz. iss
Aqua q. s. ad	oz. iv

Sig. Two teaspoonfuls in half glass of water q. i. d.

The use of tablets is somewhat less unpleasant, but fairly large amounts of water should be taken at the same time. The use of sodium bicarbonate is believed by some clinicians to lessen gastric irritation, but Hanzlik has shown that there is little reason for employing it when the neutral sodium salicylate is given. It does hasten the elimination of salicyl in the urine which may interfere with the desired effect.

The use of other salicyl derivatives has been tried in an effort to minimize gastric irritation. There is no difference between the natural and synthetic forms of the drug. Strontium salicylate and combinations of acetylsalicylic acid with calcium and other salts are stated to be somewhat less irritating, but carefully controlled series of cases have not been reported. Acetylsalicylic acid (aspirin) is probably more irritating to the gastric mucosa and does require the use of sodium bicarbonate when given in large doses.

The indications for the salicylates as compared with those for the sulfonamide group may be briefly discussed. In cases of definite intraocular infection with pyogenic organisms, as after a penetrating wound, an operation or in the course of a general infection, reliance must be placed on the definitely bacteriostatic effects of the sulfonamides. This will also be true in cases of very severe iridocyclitis, especially when accompanied by hypopyon. In the more common types of acute iridocyclitis, in which complete relief is usually obtained by the salicylates, these drugs will be preferred because of their freedom from toxic reactions. An advantage of the salicylates is their immediate relief of pain, which is seen with the sulfonamides only after the inflammation is under control. There is no objection, according to Bliss and Long, to giving moderate doses of the salicylates with sulfanilamide during the first few days, chiefly for the relief of pain. In sympathetic ophthalmia, as previously stated, few reports of sulfonamide therapy are available, while results with the salicylates seem to be definite in many cases. On account of the seriousness of the condition, however, the tendency seems justified to try the sulfonamides in cases which do not respond promptly to salicyl therapy.

Cinchophen and Neocinchophen have been used as substitutes for the salicylates in cases of intolerance or in cases which did not respond to the salicylates. An increasing number of reports have appeared indicating severe and even fatal damage to the liver from cinchophen, while in a num-

ber of other cases severe dermatitis has followed its use. Since the dosage necessary to relieve symptoms is about the same as that of the salicylates, it must be considered, as a rule, unsafe to use these drugs in inflammations of the eye. If they are employed, a dose of 5 grains should be given, followed by a wait of twenty-four hours to determine if signs of an idiosyncrasy appear.

Other drugs which have been used *systemically* with the object of combating infection include *hexamethylenamine* (urotropine), *tartar emetic*, the *arsenicals* and *sodium gold thiosulphate*. *Hexamethylenamine*, principally employed in infections of the urinary tract, has been used in certain ocular infections, including sympathetic ophthalmia. It is only effective in an acid medium and, hence, cannot be expected to exert a bacteriostatic effect in the blood or tissues. *Tartar emetic* is a specific in certain protozoan diseases, including lymphogranuloma venereum, which occasionally is associated with uveitis. In this condition proper dosage undoubtedly exerts a curative effect in many cases. It has been employed by Julianelle in the treatment of trachoma. The results of such treatment, compared with those of other methods, will be discussed later. (See page 227.)

The *arsenicals* have been employed in many types of infection with the idea of killing or inhibiting the etiological agent, usually one of unknown nature. In ocular diseases associated with various forms of dermatitis, beneficial effects are ascribed to the use of Fowler's solution (liquor potassii arsenitis) by mouth, and to that of sodium cacodylate by intramuscular injection. The dose of Fowler's solution is 3 minims once or twice a day; that of sodium cacodylate is 1 to 2 grains by injection. Both drugs produce toxic effects in certain persons, and their use does not have as definite a basis, either clinically or theoretically, as is the case with other forms of chemotherapy. Arsphenamine and its derivatives have been employed in certain non-luetic diseases. There is no doubt of their effect in Vincent's angina, which

rarely involves the eye. There have been a number of reports indicating the value of arsphenamine in sympathetic ophthalmia. Morax and other French observers were fairly enthusiastic in their claims, and the drug is employed in this condition by a few American ophthalmologists in preference to sodium salicylate. However, few reports on this subject have appeared in recent years. The same dosage and number of injections is employed as in the early treatment of syphilis.

Solutions containing *gold* have been employed in the treatment of tuberculosis, especially in tuberculous diseases of the skin. The idea that gold affects the tubercle bacillus directly has been abandoned by most clinicians, but cases of clinical improvement in certain chronic and intractable conditions were numerous enough to encourage use of the method by some ophthalmologists. Benedict and O'Leary have reported on the use of *sodium gold thiosulphate* in cases of chronic uveitis which had resisted other forms of treatment. While their chief indication for such treatment was uveal tuberculosis, they employed the method also in certain cases which showed no definite evidence of tuberculosis. Among 28 cases of central chorioretinitis they observed improvement in 11, while among 8 cases of definite choroidal tuberculosis 4 showed improvement. The treatment, according to these authors, has no effect on pain or inflammatory symptoms, and improvement ascribed to the drug is very slow, appearing *only after weeks or months and continuing after treatment* is discontinued. By keeping the dosage low and stopping treatment on the first symptoms of intolerance, undesirable reactions reported by other authors, which have resembled those following the arsenicals, were almost wholly avoided in their series of cases. No undesirable ocular reactions were seen which could be ascribed to the drug. They apparently observed no instances of gold-staining of the cornea, such as have been reported in a very few cases from European clinics. The routine now employed by Benedict

and O'Leary* is as follows: Treatments are given intravenously, the preparation of Schamberg and Wright being employed. The initial dose is 10 mg. and dosage is increased by 5 mg. at each injection to a maximum of 50 mg. Injections are given twice a week and thirty injections constitute a course. After a rest of two months another course may be given if desired.

The author's personal feeling is that gold therapy rests upon a very doubtful foundation and that its results are difficult to interpret in view of the great variability in the course of the conditions for which it has been employed. The clinical observations of Benedict, however, cannot be overlooked, and in the type of chronic uveitis described which has resisted all other forms of therapy, a trial of the method may be justified.

There is one aspect of therapeutics which should be axiomatic, but is so often overlooked, with unpleasant results, that a reminder of its importance seems in place. This is the principle that *proper therapy should increase the patient's confidence in his physician*, and that nothing avoidable should be done which will lessen that confidence. Patients consult the ophthalmologist to make them see better and when atropine or homatropine is employed it is much simpler to give warning that the pupil will be dilated and near-vision will be blurred before this occurs than to explain it to a highly alarmed patient afterwards. Patients seek relief from pain and when a miotic is given in acute glaucoma, the cramping pain which may be expected should be mentioned. The first treatment with copper sulphate or silver nitrate has caused many patients to seek other advice when a word of warning and the use of a weak local anesthetic for a few hours afterwards would have prevented this. The chemosis following dionin and the tinnitus or even deafness following sodium salicylate are other phenomena which are naturally alarming

* *Personal communication.*

to anyone who is not informed that they are unavoidable and necessary effects of the treatment prescribed.

The following list gives the drugs and extracts, listed by their common names, most used in ophthalmology, with the usual dose of each, classification by supposed effect and the principal conditions in which they are employed.

Acetic acid: 1 per cent by instillation Alkali burns of cornea and conjunctiva.

Acetyl-cholin (acecholine) (tissue extract): 0.1 to 0.3 gm., subcutaneously. Closure of central retinal artery.

Acetyl salicylic acid (aspirin): 50 to 100 grains a day. Iritis and iridocyclitis.

Adrenalin chloride: Preparation of epinephrin. 1 to 1000 solution by instillation as local vasoconstrictor. 1 to 2 per cent solution by instillation in glaucoma.

Afenil (calcium and urea compound): 10 cc. of 10 per cent solution by vein. Vernal conjunctivitis.

Aminglaukosan: 10 per cent solution of histamine for instillation. Powerful miotic. Acute glaucoma. (Caution.)

Ammoniated mercury: 1 to 3 per cent ointment. Antiseptic Blepharitis.

Ammonium tartrate: 5 per cent neutral solution by instillation. Lime burns of cornea and conjunctiva.

Amyl nitrite: 3 minims in pearls for inhalation. General vasodilator. Closure of central retinal artery.

Amytal (sodium amytal): 3 grains by mouth as hypnotic.

Antidiphtheritic serum: 5000 to 10,000 units by veins in diphtheritic conjunctivitis.

Antimeningococcic serum. (Also meningococcic antitoxin.) See p. 127.

Antipneumococcic serum: See p. 128.

Antitetanic serum: 1500 to 2000 units intramuscularly. After dirty wounds of lids or globe.

Aolan: 5 to 10 cc. of prepared ampoule intramuscularly. For foreign protein reaction.

Argyol: 10 per cent solution. Mild antiseptic. Conjunctivitis.

Aristol (thymol iodide): Powder antiseptic. As a dusting powder after operations. To fill cavity after destruction of lacrimal sac.

Arsphenamine (salvarsan): 0.15 to 0.9 gm. by vein. Syphilis. Sympathetic ophtbalmia.

Atropine sulphate: 0.5 to 2 per cent solution or ointment. Mydriatic and cycloplegic. Iritis, keratitis, uveitis, penetrating wounds.

Bismuth: Various salts and compounds for intramuscular injection. Syphilitic ocular affections.

Boracic acid: Saturated solution. Mild antiseptic for irrigation of conjunctival sac. 40 grains of the crystals added to 1 ounce of collyria is used as a preservative.

Brilliant green: 2 per cent tincture for application to lids. Antiseptic. Blepharitis.

Butyn: 1 to 2 per cent solution by instillation. Local anesthetic. Substitute for cocaine in glaucoma, removal of foreign bodies.

Calcium chloride: 5 grains, t. i. d., by mouth. Glaucoma. Vascular lesions of retina. Vernal conjunctivitis. Intraocular hemorrhage.

Calcium gluconate: 10 cc. of 10 per cent solution by vein or intramuscularly. 30 grains, t. i. d., by mouth. Same indications as calcium chloride.

Calcium lactate: 30 grains, t. i. d., by mouth. Same indications as calcium chloride.

Carotene-in-oil: Chemical precursor of vitamin A. As effective as vitamin A in deficiencies. (About 7500 units per cc.). 40 to 60 drops a day by moutb.

Caseosan: 5 to 10 cc. of ampoule intramuscularly. For foreign protein reaction.

Cevitamic acid: Crystalline form of vitamin C. 50 mg. contains equivalent of 4 ounces of orange juice. One to two tablets daily in recurrent hemorrhages.

Chondroitin sulphuric acid: Tissue extract. 4 to 6 grams a day by mouth to prevent migraine.

Cinchophen (atophan): 30 grains, three to four times a day, by mouth. To combat non-specific inflammation. Iridocyclitis. Test for idiosyncrasy by giving one 5 grain dose. Danger of liver damage if administered longer than one week.

Cocaine hydrochloride: 1 to 10 per cent solution for instillation. 2 to 4 per cent for injection subconjunctivally, not more than 4 minims. Local anesthesia.

Codeine sulphate: $\frac{1}{4}$ to 1 grain by mouth or by hypo. Narcotic.

Cod-liver oil: 1 to 4 drams, t. i. d., by mouth. Contains vitamins A and D. Blepharitis, hordeola, phlyctenulosis.

Collargol: 5 per cent solution by instillation. Conjunctivitis.

Copper citrate: 5 to 10 per cent ointment. Trachoma.

Copper-sulphate: Crystal for application. 0.4 per cent solution for instillation. Trachoma.

Daturin: 1 per cent solution by instillation. Mydriatic and cycloplegic. Substitute for atropine.

Dilaudid: Opium derivative. $\frac{1}{32}$ to $\frac{1}{16}$ grain subcutaneously as narcotic.

Dionin (ethyl morphine): 1 to 10 per cent solution by instillation or subconjunctival injection. Local vasodilator. Keratitis, corneal dystrophies, incipient cataract.

Diphtheria antitoxin: *5000 to 10,000* units intramuscularly. Diphtheritic conjunctivitis or for protein reaction.

Doryl (carbaminoylcholin): Miotic. 0.75 per cent solution by instillation in glaucoma.

Duboisin sulphate: 0.25 to 0.5 per cent. Mydriatic and cycloplegic. Substitute for atropine.

Emmenin: Glandular extract containing active estrogenic substance. Headaches and other disturbances corrected with menstrual cycle or menopause. Solution may be taken by mouth.

Ephedrine: 3 per cent solution by instillation as local vasoconstrictor. 5 per cent solution by instillation for mydriasis.

Epinephrin: Official name for extracts of adrenal gland in U. S. A. Preparations also called adrenalin and suprarenin. 1 to 1000 solution of hydrochloride by instillation as vasoconstrictor, as in vernal conjunctivitis. Same by pack or injection in glaucoma. Stronger solutions by instillation in glaucoma.

Ergotamine tartrate (gynergen): $\frac{1}{250}$ grain by hypodermic or $\frac{1}{60}$ to $\frac{1}{30}$ grain, t. i. d., by mouth. Sympathetic depressor. Glaucoma.

Eserine salicylate: 0.2 to 1 per cent solution by instillation. Miotic. Glaucoma and to counteract atropine group.

Eserine sulphate: Same as eserine salicylate.

Euphthalmine: 3 to 5 per cent solution by instillation. Mydriatic. Especially for ophthalmoscopic examination.

Fluorescein sodium: 1 to 2 per cent solution by instillation (solution made faintly alkaline with sodium carbonate). To stain lesions of cornea or conjunctiva.

Fluorescein, water-soluble* 1 per cent solution in distilled water.

Glucose (hypertonic solution): 100 cc. of 50 per cent solution by vein to reduce tension in glaucoma.

Glycerin: 25 per cent added to solutions of copper sulphate. Trachoma. 100 per cent used in chemical burns of conjunctiva.

Halibut-liver oil: Contains vitamin A in concentrated form (about 49,000 units per cc.). 15 to 20 drops daily by mouth in deficiencies.

Hexyl resorcinol: Synthetic antiseptic. 1 to 2500 solution in conjunctivitis or in preparation for operation.

Holocaine (phenacaine) hydrochloride: 1 per cent solution (made faintly acid with acetic acid). Local anesthetic. *Substitute for cocaine in glaucoma, removal of foreign* bodies.

* National Aniline and Chemical Company, New York.

Homatropine hydrobromide: 2 to 5 per cent solution by instillation. $\frac{1}{50}$ grain in gelatin tablets. Mydriatic and cycloplegic. Refraction and where brief atropine effect is desired.

Ichthyol: 10 to 15 per cent ointment. Antiseptic and stimulant. Blepharitis and dermatitis.

Iodine: 3 per cent tincture for sterilizing the skin before operation. Iodine crystals, 5 grains, with tincture of iodine, 5 minims, and glycerin, 5 minims. For local application to corneal ulcers.

Levoglaukosan (linksglaukosan): 2 per cent adrenalin solution specially prepared for instillation. To lower tension in glaucoma and dilate pupils with early synechiæ.

Luminal (phenobarbital): ½ to 2 grains by mouth. Hypnotic. Preoperative or as aid to local anesthesia.

Mecholyl: Cholin derivative. Powerful parasympathetic stimulant. 10 per cent solution in chronic glaucoma. 20 per cent solution with 5 per cent prostigmine in acute glaucoma. 10 to 15 mg. by retrobulbar injection in acute glaucoma. (Caution.)

Mercuric chloride (corrosive sublimate): 1 to 5000 solution for irrigation. 1 to 5000 ointment as antiseptic. Conjunctivitis.

Mercuric cyanide: 1 to 5000 to 1 to 1500 solution. By instillation and subconjunctival injection.

Mercuric oxide (yellow oxide): 1 to 2 per cent ointment. Antiseptic. Blepharitis. For massage of corneal scars.

Mercurous chloride (calomel): Powder. Mild antiseptic. As a dusting powder in phlyctenular conjunctivitis.

Mercurochrome: 1 to 2 per cent solution by instillation. Antiseptic. Conjunctivitis. Powder for local application in serpent ulcer.

Mercury ointment: 30 per cent ointment. For inunctions in syphilis.

Metaphen: Synthetic mercury derivative. 1 to 2500 by instillation. Conjunctivitis.

Metycaine: Local anesthetic. 2 to 4 per cent by instillation.

Milk: Whole milk boiled four minutes. 5 to 10 cc. intramuscularly. For foreign protein reaction.

Morphine sulphate: $\frac{1}{12}$ to $\frac{1}{4}$ grain by hypodermic. Narcotic, analgesic. Preoperative and postoperative, especially in squint operations.

Naphthalan: 1 per cent ointment. Antiseptic. Blepharitis.

Nembutal (pentobarbital sodium): 1.5 to 3 grains as hypnotic.

Neoarsphenamine (neosalvarsan): 0.15 to 0.9 gm. by vein. Spirocheticide. Syphilis.

Neocinchophen (tolysin): 30 grains, three to four times a day, by mouth. To combat non-specific inflammation. Iridocyclitis. Same caution as for cinchophen.

Neosilvol: 10 per cent solution. Mild antiseptic. Conjunctivitis

Nipasol (p-oxybenzoic acid): 0.04 per cent solution of acid or 0.1 per cent solution of its sodium salt as preservative for alkaloids.

Noviform: Powder antiseptic. To dust in conjunctival sac after injury or operation.

Novocaine hydrochloride: 1 to 4 per cent solution by injection. Local anesthetic.

Nupercaine: 1 to 1000 to 1 to 500 solution by instillation. 1 to 500 ointment. Local anesthetic. For prolonged anesthetic effect, as after foreign body removal.

Optochin (ethyl hydrocuprein): 1 to 2 per cent solution by instillation. Bactericide for pneumococci. Conjunctivitis. Powder for application in serpent ulcer.

Ovarian extract: 5 grains, t. i. d., by mouth. For ocular disturbances or migraine associated with menstrual disorders. Now replaced by one of the potent extracts. (See p. 75.)

Pontocaine: Local anesthetic. 0.5 per cent by instillation.

Parathyroid hormone (parathormone): 20 to 30 units, one to three times a day. Hormone of parathyroid gland. In tetany parathyreopriva, to prevent or control cataract.

Phenacaine: Official name of holocaine. Local anesthetic. 1 per cent solution by instillation. 1 per cent ointment.

Pilocarpine nitrate: 1 per cent solution. Miotic. Glaucoma and to counteract atropine group.

Pituitary extract (extract of whole gland): 1 to 3 grains, t. i. d., by mouth. In acromegaly or symptoms of pituitary insufficiency (of doubtful efficacy).

Pituitrin (posterior lobe extract): 5 minims by subconjunctival injection. Smooth muscle stimulant and vasoconstrictor. Glaucoma. 1 cc. subcutaneously for pain in herpes zoster.

Potassium ferricyanide: 2 per cent solution mixed with 12 per cent sodium thiosulphate in localized argyrosis.

Potassium iodide: Saturated solution. 5 to 60 minims, t. i. d., by mouth. Syphilis, vitreous hemorrhages, blastomycosis, sporotrichosis.

Progynon: Extract containing active estrogenic substance. 5000 to 10,000 units subcutaneously in disorders associated with the menstrual cycle or menopause.

Prostigmine: hydrobromide: Parasympathetic stimulant. Miotic 3 per cent solution in chronic glaucoma. 5 per cent solution with 20 per cent mecholyl in acute glaucoma.

Protargol: 2 per cent solution. Antiseptic and astringent. Conjunctivitis.

Resorcin: 0.5 per cent solution. 0.5 to 1 per cent ointment. Antiseptic and local stimulant. Blepharitis and chronic conjunctivitis.

Riboflavin (vitamin G): 3 to 5 mg. daily by mouth, 1 mg. by vein. In rosacea keratitis and certain other cases of keratitis and scleritis.

Scopolamine hydrobromide: 0.2 per cent solution. Mydriatic and cycloplegic. Substitute for atropine.

Silver acetate: Antiseptic. 1 per cent solution (saturated solution) for prophylaxis in new-born.

Silver nitrate: 1 to 2 per cent solution. Antiseptic and astringent. Prophylaxis at birth. Conjunctivitis.

Sodium bicarbonate: 5 per cent solution for instillation. Chronic conjunctivitis.

Sodium bromide: 16 grains, q. i. d., by mouth. Sedative. Postoperative in nervous patients.

Sodium nitrite: Vasodilator. 1 grain t. i. d. by mouth in spasm of retinal arteries. 1 cc. of 10 per cent solution by vein in retrobulbar neuritis and certain conditions attributed to angiospasm.

Sodium salicylate: 30 grains, three to five times a day, by mouth. To combat non-specific inflammation. Iridocyclitis, sympathetic ophthalmia.

Sodium sulphite: Solvent for tear gas. 50 per cent alcoholic solution in burns of skin with tear gas. 0.4 per cent solution in 25 per cent water and 75 per cent glycerin in burns of conjunctiva with tear gas.

Sodium thiosulphate: 1 gm. in 10 cc. distilled water by vein in arsenical reactions, especially loss of vision after use of tryparsamide. 12 per cent solution with 2 per cent potassium ferricyanide by injection for localized argyrosis.

Sorbitol: Hypertonic solution. Same indications and dosage as glucose.

Stannoxyl: Tablets containing 47.5 per cent tin and 7.5 per cent tin oxide. 2 to 8 tablets daily. Staphylococcic infections. Hordeola.

Strontium salicylate: Same dosage and indications as sodium salicylate.

Sulfanilamide: Bacteriostatic agent. For dosage see pp. 102 to 103. For local use 5 per cent ointment. In trachoma, inclusion blenorrhea, gonococcal conjunctivitis, intraocular infection, pyogenic infections of the adnexa.

Sulfapyridine: Bacteriostatic agent, especially in pneumococcic infections. Also in gonococcic and meningococcic infections. For dosage, see page 106.

Sulfathiazole: Bacteriostatic agent, especially in pneumococcic and staphylococcic infections. For dosage, see page 107.

Sulpharsphenamine: Arsenical. 0.15 to 0.6 gm. by vein or intramuscularly in syphilis, especially the latter method in children.

Suprarenin bitartrate: Preparation of epinephrin. Powder in ampoules to which 2.5 cc. of water is added to make a 2 per cent solution. By instillation in glaucoma or iritis with posterior synechiæ.

Theelin: Extract containing active estrogenic substance. 5000 to 10,000 units subcutaneously. In headaches or other disturbances associated with the menstrual cycle or menopause.

Thiamine chloride (vitamin B_1): 16,000 units by vein, 20 to 30 mg. by mouth. In toxic amblyopia, optic neuritis and retrobulbar neuritis. See page 332.

Thyroid extract: $\frac{1}{4}$ to 1 grain, once to three times a day, by mouth. In ocular conditions having a supposed relation to thyroid dysfunction.

Thyroxin: Crystalline principle of thyroid gland. $\frac{1}{120}$ grain. Same indications as thyroid extract.

Tryparsamide: Pentavalent arsenical. Used in syphilis of central nervous system. Contraindicated in presence of optic atrophy. Caution, watch for damage to optic nerves. 1 to 3 gm. by vein.

Tuberculin: Koch's old tuberculin, Deny's bouillon filtré, tebeprotein, other preparations. Subcutaneous injection of dilutions. $\frac{1}{50,000}$ to $\frac{1}{5,000}$ mg. as initial dose.

Turpentine: 10 per cent in oil. 1 cc. intramuscularly. A substitute for foreign protein therapy. Sympathetic ophthalmia, vitreous infection.

Typhoid vaccine: Mixed typhoid and paratyphoid vaccine. Dilute to give 30,000,000 to 70,000,000 organisms by vein. For foreign protein reaction.

Urotropine (hexamethylenamine): $7\frac{1}{2}$ to 15 grains by mouth, t. i. d. Antiseptic. To combat non-specific infection.

Viosterol: Irradiated ergosterol. Standardized 250 D. 10 to 20 gtt. a day by mouth. Contains vitamin D.

Vitamin A Concentrate: Contains 25,000 units per capsule. 1 to 2 capsules daily in deficiencies.

Vitamin B: (See p. 80.)

Vitamin C: (See Cevitamic acid.)

Vitamin D: (See Viosterol.)

Zinc chloride: 0.2 per cent solution for instillation. Astringent and mild antiseptic. Conjunctivitis. 2 per cent solution for application to lids in Morax-Axenfeld conjunctivitis.

Zinc oxide: Official ointment in blepharitis or meibomitis. Powder or calamin-zinc oxide lotion in dermatitis of lids.

Zinc sulphate: 0.4 per cent solution. Indications same as for zinc chloride.

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CHAPTER IV.

SPECIFIC AND NON-SPECIFIC PROTEIN THERAPY.

IMMUNE SERA.

There are but few sera of this type which find any use in ophthalmic therapeutics. **Antitetanic serum** is indicated after any injury in which material likely to contain tetanus spores is carried into the lids, orbit or globe. The usual prophylactic dose of 1500 units is injected subcutaneously or intramuscularly.

Antidiphtheritic Serum.—Antidiphtheritic serum is used in the rare cases of conjunctivitis due to Bacillus diphtheriæ. In any case of conjunctivitis with membrane formation, whether or not pharyngitis is also present, this condition should be suspected and cultures made. In suspected cases an initial dose of serum may be given while awaiting the laboratory report, and if this is positive 3000 to 5000 units should be injected daily until general and local symptoms have cleared up.

Antimeningococcic Serum.—Antimeningococcic serum when administered by vein as well as intraspinally is of great value in preventing the ocular complications of epidemic meningitis, especially endophthalmitis. When once endophthalmitis has developed, it has usually been supposed that serum was powerless to prevent loss of the eye, but a recent report by Lazar on the use of the meningococcic antitoxin of Ferry shows that in a few cases seen at the onset of endophthalmitis it is apparently possible to arrest the process and preserve useful vision by intravenous use of this preparation. 3000 units are given by vein daily for a number of

days in severe cases of meningitis in addition to the amount which is given intraspinally.

As has been stated, a few dramatic recoveries from endophthalmitis in meningitis have resulted from sulfanilamide, and the combination of this drug with the specific antiserum is preferred by some clinicians.

Antigonococcic Serum.—While such sera are used in gonococcal conjunctivitis and iritis by a number of ophthalmologists, chiefly in France and Italy, there is little evidence of their superiority over non-specific protein therapy. The use of the sulfonamides apparently affords even better results.

Antipneumococcic Serum.—Specific rabbit sera are now available against thirty-six types of the pneumococcus, and if proper typing is employed the suitable serum should be useful in serpent ulcer and other infections due to the pneumococcus. The author is not aware of any large series of ophthalmic cases in which these sera have been employed. As in pneumonia, the combination of the sera with sulfapyridine might well be employed.

Convalescent Serum in Herpes Zoster.—Gunderson has reported very favorable results by the transfusion of 250 to 450 cc. of whole blood taken from persons who have recovered from herpes zoster within six to eighteen months from the time their blood is employed. He believes that ocular complications may be prevented if the transfusion is given early enough. Of his 22 cases which had already developed keratitis or uveitis when transfusion was employed, 16 or 82 per cent recovered vision of 6/18 or better, while only 4 or 18 per cent lost useful vision in the affected eye. These results he compared with those in a series of earlier cases receiving no blood, of which 40 per cent lost all useful vision in the affected eye. The effect on pain, as well as on the organic lesion, was definite in most cases. It has been proposed to use convalescent serum from varicella patients

where zoster serum was not available. Gunderson doubts the value of this serum in zoster cases, and saw no effect in one case in which it was employed.

VACCINES.

These have been chiefly used by ophthalmologists in the treatment of *recurrent hordeola* and less frequently of *ulcerative blepharitis due to the staphylococcus*. It is recognized that an autogenous vaccine is superior to the stock vaccines, and in any case in which a vaccine is to be used a culture on agar or blood agar should be made from the pus obtained from a freshly opened stye. Care should be taken not to touch the lashes or skin in making such a culture, lest other strains of staphylococcus be introduced. The vaccine made from this culture by a reliable laboratory is dispensed in a dilution of which 0.1 cc. is the initial dose. This should be given subcutaneously, and injections are made twice a week, increasing the dose by 0.1 cc. each time until fifteen to twenty injections have been given. If a general reaction is obtained, or fresh styes should appear during treatment, this is an indication of the so-called negative phase, in which the antigen has been introduced in quantities greater than can be neutralized by the body's defenses. Under these conditions the dose must be cut down to one which causes no such reaction and is increased more gradually, while the intervals between injections are increased to a week.

The method of killing the organisms for a vaccine is not without importance, and there seems to be definite evidence, as shown by Kendall, that a vaccine prepared by using the smallest amount of antiseptic necessary to kill the organisms has a more marked antigenic effect than one prepared in the usual way by heat, since it leaves the bacterial proteins practically unchanged.

The use of vaccines in cases of chronic iridocyclitis or choroiditis has been adopted by relatively few ophthalmologists. Where the cause of uveitis is presumably a focus

of infection the removal of such a focus is certainly the most important thing which can be done, when, as in the case of tonsils or dental roots, this is possible. When the infection is a chronic sinusitis or prostatitis, however, a radical cure may be impossible, and even infection from tonsils and teeth may have set up secondary foci in the lymph nodes or elsewhere, which continue to affect the ocular condition unfavorably. Under such conditions treatment by a vaccine made from the supposed focus of infection might be of the greatest value. There are a number of difficulties in the way of such treatment, however. A mixed culture is often obtained in cultures of the suspected organ from which it may be impossible to pick the offending organism. This organism again must be grown under conditions closely resembling those in the body in order that its antigenic properties may be preserved. Rosenow claims to have met these difficulties in his method of growing cultures in deep semisolid media at partial tension. He reports that pathogenic streptococci, which are the most frequent offenders, grow selectively in such a medium, and Benedict, using such cultures made from various foci, including the prostate and the female genital tract, for the preparation of vaccines, has reported excellent results in some chronic cases of uveitis. The methods are by no means standardized, and unless unusually good coöperation from the laboratory is available results are apt to be uncertain. The hope does not seem ungrounded that methods of using vaccines in such conditions may be standardized so as to be of more general value. In a recent monograph, Woods has reviewed this subject, and described a method of preparing vaccines which offers possible advantages in staphylococcic infections of the lids and conjunctiva.

In chronic conjunctivitis due to one of the toxin-forming strains of staphylococcus, Thygeson has employed *staphylococcic toxoid* with apparently good results. The systemic and local use of the toxoid is discussed on page 235.

TUBERCULIN.

Authorities on general medicine are by no means in agreement as to the value of tuberculin. A number consider it of value for diagnostic purposes, but most agree that Koch's hopes of having found a specific remedy in all types of tuberculosis have by no means been fulfilled. In tuberculosis of the eye we are dealing with a special manifestation of the disease, in which frank pulmonary tuberculosis is seldom present, and the original focus must be considered as a group of peribronchial or cervical glands which cause no symptoms, but allow the escape of organisms or toxins into the circulation which produce their principal manifestations in the eye. The most important ocular diseases which are due to tuberculosis, including the type of allergy to tuberculous toxins thought to be responsible for many cases of phlyctenulosis, will be discussed in Chapters VIII, IX, and XII.

It is known that the use of tuberculin in pulmonary tuberculosis is capable of arousing a focal reaction which may have serious results. For this reason its use in ocular complications of active pulmonary tuberculosis is usually contraindicated. *In most types of ocular tuberculosis,* however, active pulmonary disease is not present, and in clinics where many cases of ocular tuberculosis are seen *tuberculin has been and in most cases still is considered an important part of the treatment of this condition.* In spite of certain theoretical objections, enough positive clinical evidence of its value has accumulated so that patients with ocular conditions considered tuberculous, and showing positive diagnostic tests, should not be deprived of its possible benefits.

In phlyctenulosis, as will be explained, not much benefit can usually be expected of tuberculin, and this condition responds more readily to general measures than other tuberculous conditions. In sclerosing keratitis, tuberculous iritis, iridocyclitis and chorioretinitis, however, the indications

are definite and a course of tuberculin should usually be advised. In periphlebitis retinæ, which is so often of tuberculous origin, tuberculin therapy is important, but must be carried out with great caution. The larger diagnostic doses are omitted and treatment is begun with very minute doses to avoid the danger of a focal reaction which might cause permanent damage to vision.

The form of tuberculin which has been most generally employed, and with which most of the evidence in favor of tuberculin has been gathered, is *Koch's old tuberculin* (O. T.). This is a filtrate of killed tubercle bacilli to which glycerin is added, and which is supplied in concentrated form in ampoules. For diagnostic use the von Pirquet test, in which 1 drop of concentrated tuberculin is rubbed into small puncture wounds of the dermis, is of value chiefly in small children, where a positive reaction may be considered to indicate the presence of active tuberculosis. In adults a positive result is usually given by any patient who has ever had any form of tuberculous infection, so that only a negative reaction is of value as indicating the absence of the disease. Of more value is the intradermal test, with graduated dilutions of old tuberculin.

A convenient method of making up solutions of tuberculin for diagnostic and therapeutic use is the following: Five bottles containing 100 cc. of sterile normal saline are sterilized and to each bottle 0.5 cc. of phenol is added as a preservative. To bottle No. 1 is added 0.1 cc. of Koch's old tuberculin, measurement being accurately made with a tuberculin syringe. 1 cc. of this contains 1 mg. of tuberculin, and it should be labelled accordingly. (Fig. 19.)

To bottle No. 2 is added 10 cc. of bottle No. 1, 10 cc. of the salt solution having first been removed. After thorough shaking 1 cc. of this contains 0.1 mg. of tuberculin.

To bottle No. 3 is added 1 cc. of bottle No. 1; 1 cc. of this contains 0.01 mg. of tuberculin.

To bottle No. 4 is added 0.1 cc. of bottle No. 1; 1 cc. of this contains 0.001 mg. of tuberculin.

Bottle No. 5 is used as a control and contains only 0.5 cc. of phenol.

For the intradermal test 0.05 cc. of each dilution is used intradermally on the palmar surface of the forearm, injections being made 1 inch apart. If one commences with the control the same syringe may be used for all five injections, as in this

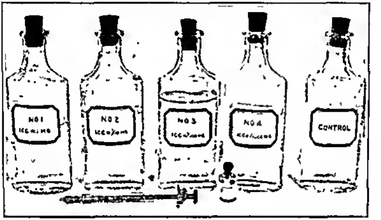

FIG 19 —Bottles for dilutions of old tuberculin and tuberculin syringe

way there is no possibility of carrying a more concentrated solution into one less concentrated. A fresh needle should be used for each injection, which is made into and not under the dermis, so that a small white wheal is produced. For the intradermal test only the local reaction is important, a general and focal reaction being seldom seen. The reactions should be read after one hour, twenty-four hours and forty-eight hours, and the dilutions giving a raised area of erythema 1 cm. or more in diameter, which persists twenty-four hours, are considered positive. The control should be negative, and if positive, indicates a sensitivity to phenol, in which case the test must be repeated with fresh solutions made without preservative.

The advantage of the intradermal test is that all dilutions may be used at once, which is economical of time, and that an idea of the relative sensitivity to tuberculin is obtained as an indication for the dosage to be employed therapeutically. Thus a patient giving a reaction to $\frac{1}{20\,000}$ mg. (No. 4) should begin with about this amount therapeutically, while if the No. 2 and No. 1 tests alone are positive a larger dose may be used at the outset. Also this method protects us against pseudoreactions due to infection, since true reactions should be more intense with the more concentrated solutions. A reaction with No. 3 or No. 2 alone is almost certainly such a pseudoreaction.

Another method of diagnosis is the *subcutaneous* injection of old tuberculin, the general and local reactions being observed and the occasional focal reactions in the eye itself being considered especially significant. The temperature should be controlled for twenty-four hours before injections and for forty-eight hours afterward, at two-hour intervals. The initial injection is usually 0.1 mg., or 0.1 cc. of bottle No. 1, except in retinal conditions where a focal reaction is especially to be feared and where the intradermal test, using only No. 3 and No. 4, is the safest method. If with 0 1 mg. no local or general reaction is obtained, 0.5 mg. is used, followed by 1 mg. Reactions with the larger doses of 5 to 10 mg. sometimes employed are of doubtful significance. Most authors require a positive local and general reaction by this method, but a local reaction alone, where the clinical picture is suggestive of tuberculosis, cannot be ignored. A certain danger of provoking serious focal reactions when employing this method undoubtedly exists. It should never be employed in retinal tuberculosis and the author prefers the intradermal method in all cases.

These solutions for diagnosis and treatment must be kept on ice and made up once a month, as the diluted tuberculin undoubtedly loses its potency more rapidly than pure tuberculin, which may be kept for a year or longer. The use of the prepared dilutions sold by some drug houses would seem to be of doubtful value for this reason.

filtrate of broth cultures, and which is preferred by Gay and others for treatment, may be prepared in the same way. This is dispensed in a preparation one-tenth as concentrated as old tuberculin. Woods advises this preparation for treatment, while he employs old tuberculin for diagnosis.

Woods has called the author's attention to the fact that most writers on tuberculosis refer to doses of tuberculin in terms of bouillon filtré instead of old tuberculin. In their works the doses of tuberculin are hence one-tenth of those given here. A different system of dilutions is also employed by certain authors, including Woods, which might bring about confusion when comparing doses employed by different ophthalmologists. It has seemed to the author least confusing to employ the term tuberculin only in one sense, that of concentrated old tuberculin, whether employed for diagnosis or treatment. If the difference in concentration is remembered and the preparation employed is specified, there should be no real cause of confusion, no matter which of the two preparations is employed.

In using tuberculin therapeutically, the initial dose should usually be small, but should not, in the author's opinion, be so small as to necessitate a too lengthy course of treatment before the larger doses are reached, as otherwise the treatment will be impractical for many patients, while in others much time may be lost at a critical point in the disease before any appreciable effect is obtained. In the technique used at the Wilmer Institute, for instance, as described by Gay, the initial dose is $\frac{1}{1,000,000}$ mg., the whole course requiring sixty-three injections given over eight to ten months, for its completion. The author prefers starting with $\frac{1}{10,000}$ mg. or $\frac{1}{5000}$ mg. in most cases, which may be considered safe except in retinal tuberculosis, where $\frac{1}{1,000,000}$ mg. is the initial dose. As stated above, a variation in the initial dose may be indicated by the results of the intradermal test. Injections are usually given twice a week, the dosage being gradually increased until 1 to 5 mg. are tolerated without a reaction. When a local reaction occurs the next injection made is smaller, usually the same as the previous dose which caused no reaction.

When a dose of 0.1 mg. is reached the intervals may be lengthened to once a week.

A general schedule of dosage, which must be varied to suit each case, follows:

Dose No	Amount of tuberculin given, mg	Amount of injection		
1	0.0002	0.2 cc. of bottle		No. 4
2	0.0004	0.4 cc.	"	No. 4
3	0.0006	0.6 cc.	"	No. 4
4	0.0008	0.8 cc.	"	No. 4
5	0.001	1.0 cc.	"	No. 4
6	0.002	0.2 cc.	"	No. 3
7	0.003	0.3 cc.	"	No. 3
8	0.004	0.4 cc.	"	No. 3
9	0.005	0.5 cc.	"	No. 3
10	0.006	0.6 cc.	"	No. 3
11	0.007	0.7 cc.	"	No. 3
12	0.008	0.8 cc.	"	No. 3
13	0.009	0.9 cc.	"	No. 3
14	0.01	1.0 cc.	"	No. 3
15	0.02	0.2 cc.	"	No. 2
16	0.03	0.3 cc.	"	No. 2
17	0.04	0.4 cc.	"	No. 2
18	0.05	0.5 cc.	"	No. 2
19	0.06	0.6 cc.	"	No. 2
20	0.07	0.7 cc.	"	No. 2
21	0.08	0.8 cc.	"	No. 2
22	0.09	0.9 cc.	"	No. 2
23	0.1	1.0 cc.	"	No. 2
24	0.2	0.2 cc.	"	No. 1
25	0.3	0.3 cc.	"	No. 1
26	0.4	0.4 cc.	"	No. 1
27	0.5	0.5 cc.	"	No. 1
28	0.6	0.6 cc.	"	No. 1
29	0.7	0.7 cc.	"	No. 1
30	0.8	0.8 cc.	"	No. 1
31	0.9	0.9 cc.	"	No. 1
*32	1.0	1.0 cc.	"	No. 1
33	2.0	2.0 cc.	"	No. 1
34	3.0	3.0 cc.	"	No. 1
35	4.0	4.0 cc.	"	No. 1
36	5.0	5.0 cc.	"	No. 1

* To avoid using such large amounts of fluid a separate dilution is usually made, containing 0.1 cc. of concentrated old tuberculin in 10 cc. of normal saline. One-tenth cubic centimeter contains 1 mg. of tuberculin, so doses 32 to 36 are 0.1, 0.2, 0.3, 0.4 and 0.5 cc. of this dilution. In certain cases it is advisable to increase the dosage no further than number 32, but to repeat this dose at two week intervals five to ten times. When sensitivity to tuberculin is high or focal reactions are especially to be feared, more dilute solutions may be prepared as follows. If 10 cc. of bottle No. 4 is added to 90 cc. of normal saline, the solution, No. 5, contains 1/10,000 mg. of old tuberculin per cc. If 1 cc. of No. 4 is added to 99 cc., the solution, No. 6, contains 1/100,000 mg. per cc.

At the Wilmer Institute the dosage is further increased up to 100 mg., while in the Meller Clinic in Vienna a dosage of 0.1 mg. is not exceeded, but this is repeated at fourteen-day intervals for at least one year.

Besides Koch's old tuberculin and bouillon filtré a number of newer methods of preparing tuberculin have come into use during the past ten years and certain advantages are claimed for the products of these methods by various observers. Von Herrenschwand, Hessberg and others are enthusiastic over the effect of the Deycke-Much partial antigens in ocular tuberculosis. These products are the result of extraction of tubercle bacilli so that the fatty components are removed completely in one product and only partially in another.

Urbanek, with the large material of the Meller Clinic in Vienna, has for some years used *Tebeprotein.* This is made by extracting cultures of human tubercle bacilli chemically, so that the pure bacterial proteins are left, with which the specific bodies of therapeutic value remain associated, while the toxic by-products present in old tuberculin are eliminated. The focal reactions produced are very slight and of short duration. Urbanek claims that he has never seen either a general or focal reaction produced by this preparation which was severe enough to produce permanent damage. In all cases a diagnostic injection of 0.1 mg. is given subcutaneously and therapeutic injections are begun with 0.0001 to 0.001 mg. When the dose of 0.1 mg. is reached after about twenty injections this is not increased, but the same dose is repeated at two-week intervals for at least a year. The doses are increased by one-half the previous dose each time, and the intervals between injections are lengthened from two days to two weeks as the dosage is increased. The results reported in his series of 500 cases were excellent.

Another variation in the use of tuberculin is the method of Ponndorff, as used in ocular tuberculosis by Rindfleisch, Goerlitz and others, especially in the German clinics. This method is based upon the idea that the antibody formation

of the skin itself is especially active and important. An area of skin, 3 to 4 cm. in diameter, is scarified and old tuberculin is applied. This is used both for diagnosis and treatment. In sensitive persons marked local inflammation and exudation results, lasting five to ten days. A moderate general reaction often occurs. In treatment the same inoculation is repeated at intervals of two to four weeks in different areas and three to eight such inoculations are given. Good results are claimed for this method by Francke in phlyctenulosis of children, in which other forms of tuberculin are difficult to use and not without danger. An obvious advantage of the method is the relatively small number of treatments which need be given to ambulatory patients coming from a distance.

Since it is so difficult to judge the effect of tuberculin in most cases as compared with that of changes in hygiene and nutrition brought about at the same time, it is even more difficult to compare the effect of one form of tuberculin with another. Hence it has not seemed profitable to examine in detail the claims of these newer preparations, but to discuss chiefly the use of old tuberculin, which is the form with which most results were obtained on which the evidence for tuberculin therapy rests. A trial of the newer agents is certainly indicated, especially by those with a large material at their disposal.

LOCAL IMMUNITY.

A great deal has appeared in the literature since 1927 concerning the application of Besredka's ideas of immunity to various ocular conditions, among them blepharitis, chronic dacryocystitis and chronic conjunctivitis. This may be considered as a form of vaccine therapy, the difference being in the way the substance is prepared and in the methods of applying it. Broth cultures of the offending organism are grown for ten days, killed by heat, and the fluid constituents of the culture are used in treatment. They contain not

only the bodies of bacteria, but also the products of their growth, which include, according to Besredka, a specific substance which he calls *antivirus*, which inhibits the growth of the offending organism. The killed culture is applied locally to the infected region. Thus in chronic conjunctivitis it is instilled in the conjunctival sac, in blepharitis it is applied to the lids on moist dressings and in chronic dacryocystitis it is injected into the sac. Killed cultures incorporated in ointments or jellies, such as have recently been put out by a number of drug houses, make use of the same principle. Reports on the use of these preparations have been in general favorable, the most striking being some reported cures of the usually intractable chronic dacryocystitis. (See Chapter XIV.)

A report by Strumia and Scarlett on the use of *bacterial lysate* in experimental staphylococcic kerato-conjunctivitis indicates that this product, containing active bacteriophage, had a favorable effect on the infections, but no more than that of heated (inactive) lysate or bacterial filtrate. In others words, the lysate apparently owed its effect, not to the active bacteriophage, but to the dissolved bacterial proteins, a conclusion which supports Besredka's views.

While these methods which attempt to produce local immunity directly should be considered as still in the experimental stage, apparently clinical results warrant further investigation. It should be said that the principles underlying the method have not been universally accepted by bacteriologists. (For a more detailed discussion of this subject, see the monograph of Woods.)

NON-SPECIFIC PROTEIN THERAPY.

This method of therapy seems to have begun with observations of the beneficial effect of intercurrent infection with accompanying fever in various diseases. Cases were also observed in which the use of antidiphtheritic serum showed

an apparently beneficial effect in diseases other than diphtheria. Out of these observations has grown, on the one hand, the inoculation with malaria of patients with parasyphilis, and on the other, the use of numerous forms of foreign protein in the treatment of various diseases, including many ocular conditions. While it seems to be recognized that fever is not the factor which overcomes the infection, as was once thought, *fever is usually a part of the group of symptoms following the injection of a foreign protein which have come to be known as foreign protein shock.* A leukocytosis, with predominance of the mononuclear cells, is part of the syndrome, and Petersen has shown that a number of tissue ferments are set free which break up bacteria and their toxins into harmless products. An increase in cell permeability also occurs, by which antibodies more readily penetrate the cells from the blood stream. This whole series of reactions results, according to Petersen, in a keying up of the body's defensive mechanism to the highest pitch. Von Szily has recently shown that one effect of foreign protein injections is the production of a definite inflammatory process in the ocular structures, the whole uveal tract showing active hyperemia and infiltration with lymphocytes. While it might be more accurate to judge of the intensity of protein shock by observation of the blood count, *fever is the symptom easiest to record, and the one by which we can most readily judge whether a reaction sufficiently intense is being produced.* Many prepared proteins, such as aolan, lactigen and omnadin, are recommended on the grounds that their beneficial effect is unaccompanied by fever, but it is the author's opinion that, though such beneficial effects are undoubtedly produced in many cases, this is simply the result of a less intense protein shock than that produced by agents causing fever. He believes that one may be more sure of the desired effect when using one of the substances which produce fever.

Of such agents, *the most generally accessible and effective are whole milk and typhoid-paratyphoid vaccines.* Since

the shock-producing properties of milk probably depend in large part, as Barkan has shown, on its bacterial content, certified or pasteurized milk is less valuable than poorer grades of milk or pasteurized milk which has been incubated for four to six hours, so that its bacterial content is increased. Such milk is boiled four minutes, cooled and injected intramuscularly. While this amount of heat does not kill the spore-bearing organisms present, these apparently have no pathogenicity when injected, and the non-spore-bearing organisms, which might produce local abscesses, are killed. Milk is especially suitable for the treatment of ophthalmia neonatorum, since the injection of 1 to 2 cc in new-born infants almost always causes a definite reaction, with fever of 100° to 103° F. It may also be used in adults with gonorrheal conjunctivitis, iridocyclitis, choroiditis, optic neuritis and keratitis. Here much larger doses must be given, 8 to 12 cc. for persons of average weight, the dosage being increased according to the reaction obtained. In general, *the best interval between injections is two days, that is, with two free days between injections.* This will depend on the reaction, and in critical conditions the next injection may be given when the patient has been free of fever for twenty-four hours; or if the blood count is being followed, when this has returned to normal for the same length of time. Usually after the first few injections reactions are slight or absent, and it is doubtful if much benefit is obtained from more than five or six injections, though the method of a larger number of small injections is preferred by some observers.

While large enough injections of milk will usually cause a definite reaction, some patients fail to show any fever following such injections, and hence in the more serious of the conditions mentioned, and especially in sympathetic ophthalmia, it seems best to make use of the typhoid-paratyphoid vaccine, with which, as Allen has shown, the amount of reaction may be more definitely predicted from the dose employed. In adults, this method has in general come to

replace the use of milk. Such injections, *when made intravenously*, are much less painful than milk injections and produce no painful local inflammation. For intravenous injections the doses are much smaller than for the usual subcutaneous immunizing injections, and the dosage must be accurately measured lest dangerous reactions occur. It is best to commence with 30 million organisms, which will cause fever of 100° to 101° F. in most patients. This is increased to 40 and then to 50, 60 or 70 million in later injections, depending on the resulting reaction. Allen speaks of using much larger doses, over 100 million organisms in some cases, and such doses are advisable in patients who do not react to smaller ones.

There is, unfortunately, considerable variation in the potency of commercial vaccines, regardless of their reported bacterial count. With some vaccines, much larger doses than those mentioned will be necessary to produce a febrile reaction. It is best to choose a vaccine with which the reactions correspond roughly to those described.

For children or small patients the doses are correspondingly smaller, and the vaccine is never employed in infants. To measure such doses a tuberculin syringe is necessary. The ordinary vaccine contains 1000 million organisms per cubic centimeter; 0.1 cc. of this is drawn up in the syringe, which is then filled to 1 cc. with normal saline and the solution mixed by means of an air bubble; 0.2 cc. of this solution will then contain approximately 20 million organisms, 0.4 cc. 40 million, etc.

A typhoid-para-typhoid preparation designed especially for intravenous use has recently become available.[1] This is made in two dilutions so that 1 cc. of No. 1 contains 50 million organisms, while 1 cc. of No. 2 contains 100 million organisms. The initial dose of 30 million organisms is given by 0.6 cc. of No. 1 and increased doses are

[1] Lederle laboratories.

made accordingly. Use of this preparation avoids the trouble of making a dilution, but in the author's experience considerably larger amounts are required to produce a satisfactory reaction than would be indicated by the stated bacterial content. Intervals between injections and the number of injections are in general the same as those described for milk injections.

Key, Verhoeff and others have insisted on the especial value of *antidiphtheritic serum* which in large doses brought about some remarkable results in Verhoeff's cases of sympathetic ophthalmia. Verhoeff advises using 16,000 units a day in this condition, while Key in cases of serpent ulcer used 2400 to 3200 units every two to three days. The disadvantages of using horse serum for therapeutic purposes are obvious. An intradermal test must be made for sensitivity to avoid the occurrence of dangerous or fatal anaphylactic shock in patients who have previously used horse serum in any form, while in using the serum the patient is made sensitive to horse serum, which may be a cause of serious inconvenience in later life.

Similar enthusiastic claims have been made by Vila Coro and others for the use of *autoserum*. Five to 10 cc. of blood are removed from the patient's vein and either the whole blood is immediately reinjected intramuscularly, or the clot is allowed to separate and the serum is reinjected. The results of this method, which often causes no febrile reaction, are claimed to be superior to those of foreign protein injections, especially in sympathetic ophthalmia. The reaction to such injections, according to Freund, is due to the formation of certain split-products in blood, as soon as it is removed from the vessels, which act as mild toxins on reinjection, producing the same type of inflammation in the eye and other organs, as von Szily has shown, which results from the injection of any foreign protein. Wick has compared the effects of autoserum with that of other protein injections,

checking the blood count, temperature and effect on the condition treated in a large series of cases. He found the effect of autoserum to be no different from that of other proteins, except that fever less often resulted, in only 4.7 per cent of cases. *Thus there seems to be no reason for ascribing to autoserum the remarkable advantages claimed by some authors, while the conditions of administering it make it much less convenient than milk and typhoid vaccines.*

INTERFERENCE THERAPY.

This is the name used by Blatt for the artificial induction of one infection for the purpose of favorably affecting another. The classical example of this is the use of malaria in paresis and tabes, which is discussed in Chapter XII. Blatt has used vaccination against smallpox for the same effect in conditions of severe iridocyclitis and postoperative inflammation, and has seen favorable results which he is sure can be ascribed to the method. In America, where the general population is, or should be, immune to the cowpox virus, the method will seldom be applicable, and the use of other inoculations, such as that of relapsing fever, will seldom be considered. Recent reports indicate that vaccination with cow-pox virus, even in previously vaccinated persons, is of value in preventing recurrent attacks of herpes.

THE FIXATION ABSCESS.

While not a form of protein therapy, the effects of this procedure are probably not unlike those of foreign protein injections. One cubic centimeter of a 10 per cent solution of turpentine in oil is usually employed, which is injected subcutaneously beneath the pectoral or abdominal skin. This results in a sterile abscess, which may reach a surprising size, and which, besides the stimulation to leukocyte formation by the entire hematopoietic system, probably also allows the continuous absorption into the blood stream of

protein split-products and cellular enzymes which have similar effects to those following foreign protein injection. The abscess forms in the course of two to three days after injection and is allowed to develop without incision until the skin over it becomes tense and perforation is threatened. It may be repeated three to four times if necessary. This method was used before the days of non-specific protein therapy in certain severe ocular conditions, especially post-operative or post-traumatic infections and sympathetic ophthalmia. In the hands of excellent clinicians it has occasionally been used with apparently good effect in similar conditions which were not showing a satisfactory response to other agents and apparently there is a place in our therapy for the method.

The direct elevation of the body-temperature by means of diathermy or air-conditioned cabinets has been used for various ocular conditions in place of foreign protein therapy. For a discussion of the method and its indications, see page 160.

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CHAPTER V.

PHYSICAL THERAPY.

While always depending to some extent on such physiotherapeutic agents as heat and cold, ophthalmologists in general have been rather slow to make use of the modern agents of physiotherapy, such as ultra-violet light, diathermy roentgen-rays and radium. This conservatism has probably depended largely on a very proper fear of possible damage to the delicate structures of the eye, the cornea, lens and retina, by these agents. Such possibilities of danger undoubtedly exist, and it is only within recent years that we are able to say just what these dangers are, to arrange proper dosage and filtration so that they may be avoided, and to decide with some approach to certainty which conditions are definitely benefited by these agents. This should mean only conditions in which phototherapy or radium, for example, offer advantages not enjoyed by the agents previously used, as needless expense and loss of time by both physician and patient should not be incurred by using more complicated methods and instruments for the treatment of conditions which are satisfactorily relieved by simpler means.

PHOTOTHERAPY.

In using light on the eye or adjacent structures there are several factors which make the effects different from those of light applied elsewhere in the body. Most important of these is the transparency of the ocular media, which allows access of certain kinds of light to the deeper structures and which may be impaired by too great a dosage of active rays. *The normal cornea **absorbs 50 per cent** of the longer infra-red rays, between 18,000 and 16,000 Angstrom units, the other half being absorbed by the lens. Between 16,000 and*

13,000 Angstrom units the cornea absorbs almost all the light, while from 13,500 down to the beginning of the visible red rays at 7700 an increasing amount is transmitted, reaching 100 per cent for the rays of the visible spectrum, 7700 to 4000. *In the ultra-violet region it absorbs practically all rays below 2950.* The aqueous and vitreous transmit all rays which pass the cornea. *The lens, besides absorbing most of the longer infra-red rays which pass the cornea, absorbs 25 per cent of rays between 13,500 and 11,000, all the ultra-violet rays between 2950 and 3200 and part of those between 3200 and 4000.* These ranges of absorption are important,

Type of ray	Cosmic rays	Gamma rays	Alpha & Beta rays	Roentgen rays	Grenz rays	Ultra-violet rays	Visible rays	Infra-red rays	Hertzian rays (short radio waves / long radio waves)	Alternating current waves
Wave length	Less than 0.1 A U*	0.1 to 0.7 A U	**	0.3 to 2.0 A U	About 2 to 3 A U	10 to 3800 A U	3800 to 7800 A U	8000 to 100 000 000 (1 cm)	1 cm to 10 000 meters	10 000 to 10 000 000 meters

* Angstrom units
** These parts of energy cannot be designated by wave length as they are radio active particles. Their properties correspond to this place in the spectrum.

FIG 20.—Distribution of radiant energy in the electro-magnetic spectrum.

since it is only the absorbed light which is effective, or in larger doses harmful. It is found, as might be expected, that the cornea is especially sensitive to ultra-violet light. It is sensitive not only because of its absorption, but because of its rich supply of nerve endings, and this sensitivity is the second factor which must be considered as peculiar to the eye. When the cornea is exposed to a source of ultra-violet light of sufficient strength an abiotic reaction begins after six to eight hours, with swelling and irregularity of the corneal epithelium and the formation of vesicles. If the exposure is longer the epithelium is completely desquamated, the corneal corpuscles show fragmentation of their nuclei and eosinophil cells appear in the cornea. This occurs, of course, only with exposures much longer than those which should be used for therapeutic purposes. Even a slight abiotic reaction over a large area of cornea is intensely painful.

Such a reaction is the real basis of photophthalmia or snow-blindness and may occur in typical form after accidental exposure to the flash of an electric arc.

It was formerly believed that snow-blindness was due to the effect of ultra-violet light on the retina. From what we know of the absorption of ultra-violet by the cornea and lens, it is apparent that only the longer ultra-violet rays between 3200 and 4000, and only part of these, ever reach the retina and changes in the retina as a result of these rays have not been shown to occur experimentally. The retinal changes produced in rabbits by Birch-Hirschfeld were chiefly in those from which the lenses had been removed, and after much longer exposure than is ever used clinically. *Large doses of infra-red rays, on the other hand, may cause injury to the retina*, and this is what occurs occasionally after looking at an eclipse of the sun, when atrophic changes in the central retina may later be seen with the ophthalmoscope.

The ultra-violet rays which pass the cornea may, in large doses, have the same effect on the epithelium of the lens capsule as on that of the cornea, and Duke-Elder warns against this in using phototherapy. Apparently the only clinical reports of cataract after phototherapy are the 2 cases of Scheerer, and in these cases some roentgen-ray treatments had also been given. It has been shown in the clinic of Vogt that very large doses of ultraviolet are tolerated by the lens without any opacity developing. In the same work, however, it was found that the infra-red rays which pass the cornea did produce lens opacities. It is to guard against this that the source of light used for phototherapy must be seriously considered.

For general irradiation of the body the sources of light chiefly employed are the mercury-vapor lamp and the carbon arc. The mercury-vapor lamp emits a light characterized by bright lines of transmission in certain regions of the spectrum, while the carbon arc emits a continuous spectrum which more nearly resembles that of the sun.

The object of general irradiation is to produce a mild skin reaction which is accompanied by changes in the blood and tissues resembling in some ways those occurring in foreign protein shock. The natural defenses against infection are increased by such a reaction and certain infections, including those of the eye, tend to heal more rapidly. *Tuberculous uveitis, sclerokeratitis* and *phlyctenulosis* are among the conditions in which

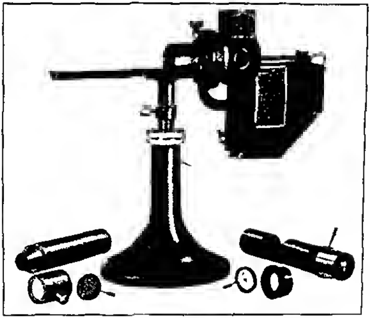

FIG. 21.—Birch-Hirschfeld irradiation lamp with uviol filter and quartz lens

such treatment seems to be of value. At Moorfields Hospital, according to Duke-Elder, one-third of the body surface is irradiated at each sitting. The mercury vapor arc is first employed, the dose being found which will produce a slight erythema. This is repeated on other areas two or three times a week for fifteen treatments. After this, five treatments are given with a carbon arc light which is richer in long ultra-

violet rays and has a more penetrating effect. After two or three weeks of rest, another course is given if necessary. The eyes must be covered by dark glasses during such treatments, to avoid painful and possibly harmful abiotic reactions.

Local Phototherapy.—In local treatments to the eye with ultra-violet light the instrument chiefly employed in European clinics and which the author has employed is the *Birch-Hirschfeld irradiation lamp* (Fig 21) This is a

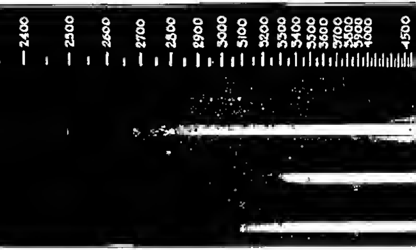

Fig 22—Spectral transmission of Birch-Hirschfeld irradiation lamp (Courtesy of Dr F Lowell Dunn) 1 Carbon arc with quartz condensers only Transmission to 2400 Angstrom units 2. Carbon arc with condensers, uviol filters and copper sulphate filter Transmission to 3100 Angstrom units 3 Carbon arc with condensers and uviol filter only Transmission to 2900 Angstrom units.

carbon arc with a quartz lens system, one lens being movable so that a fine bundle of light can be focussed on the corneal lesion. A filter of uviol glass absorbs most of the visible rays which produce dazzling and a considerable portion of the ultra-violet as well. It transmits some of the ultra-violet, however, down to 2850 Angstrom units. (Fig. 22.) The cell used by Birch-Hirschfeld containing copper sulphate solu-

tion may well be dispensed with as it further limits the amount of ultra-violet transmitted. Distilled water may be employed in the cell or the light may be employed without any cooling solution. With this apparatus the light is focussed on the lesion for five to ten minutes, this dosage being insufficient to cause erythema, as a rule. It must be kept in focus by the surgeon or an assistant, as slight movements of the head or eye will remove the lesion from the area of effective radiation. Other filters such as the Corning Glasses No. G984B or G986A transmit more ultra-violet, and with them the periods of treatment may be considerably shortened.

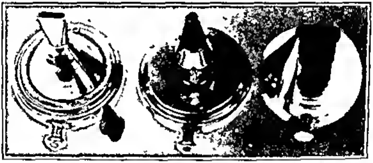

FIG 23 —Coulter's ophthalmic applicators for use with mercury vapor arc light.

The *mercury vapor arc* may also be used in local treatments to the eye, but with this more care is necessary to avoid painful reactions. Quartz applicators may be employed or the special applicators of Coulter which limit the irradiation to the desired area. (Fig. 23.)

The object of local phototherapy is to stimulate the local mechanisms of defense and healing and possibly to obtain inhibition or death of the infectious agent. Numerous reports have appeared on local phototherapy in ophthalmic conditions but the results are difficult to evaluate. It may be said the indications for local phototherapy have become more and more limited with the development of other thera-

peutic procedures and that most ophthalmologists make no regular use of the method. In spite of its waning popularity, the author must testify to his belief that local phototherapy does hasten healing in certain conditions.

As would be expected from the very slight penetration of ultra-violet rays, these conditions are chiefly corneal ulcers of the most superficial type. *Dendritic keratitis* seemed to respond best to such treatment, most cases healing after two to five, and one after a single treatment with the Birch-Hirschfeld lamp. It is true that iodine was also employed in most of these cases, but a fairly definite impression was formed that healing was more rapid and scar formation more insignificant when the light was employed. In the author's cases the areas to be treated were first stained by 1 per cent fluorescein or 1 per cent rose bengal, following Passow's evidence that organisms or, in this case, the virus are in some way "sensitized" by these dyes to the action of light. In *degenerative ulcers* at the site of previous scars, *trachomatous ulcers* and *superficial catarrhal ulcers* the light seemed to be of value, although in the latter condition chemical treatment is nearly always rapidly effective.

In serpent ulcer, phlyctenulosis and deep keratitis, in spite of certain favorable reports, a dependence upon local phototherapy cannot be advised by the author. Attempts to treat trachoma, blepharitis and other conditions of the lids and conjunctiva by this method have also been abandoned in favor of more efficacious methods.

THERAPEUTIC USE OF HEAT AND COLD.

The usual therapeutic use of heat is limited to degrees low enough to avoid damage to the tissues. By *such amounts of heat an active hyperemia is produced which is of value in many conditions.* Pain is often relieved, products of inflammation are absorbed and greater amounts of antibodies are brought to the diseased organ with an increase in local resistance to infection. Hence *heat is employed in most conditions of the*

eyes and adnexa due to infection and accompanied by swelling and exudation. *Heat is contraindicated in conditions accompanied by intraocular hemorrhage,* during the stage when fresh bleeding is likely to occur. In the early stages of conditions accompanied by extreme swelling of the lids and conjunctiva, heat is usually inadvisable. When the period of acute edema is over, however, heat is often of aid in reducing the swelling.

Cold, on the other hand, *produces constriction of the small vessels and hence lessens the swelling which accompanies the early stages of infection or reaction to trauma.* The edema of the lids and conjunctiva which is present in early gonorrheal conjunctivitis may be greatly lessened by applications of cold during the first few days. This makes it possible to evert the lids for treatment and protects the cornea from pressure which might injure its vitality. Following crushing injuries or operations the same indications for cold exist. *It is especially useful after operations on the ocular muscles, evisceration of the globe and expression of the folds in trachoma.* In early intraocular or subconjunctival hemorrhages or in simple ecchymosis of the lids, cold may cause enough vasoconstriction to stop the bleeding. Absorption of the resulting hematoma, however, after the danger of fresh bleeding is over, is aided by the use of heat. In acute glaucoma, cold is generally employed, chiefly for its effect on the accompanying pain. Even in iritis and other inflammatory conditions where heat is usually employed, pain may be aggravated by heat, and in such cases the use of cold for short periods may be preferable. On account of the danger of injuring the cornea it is not advisable to employ extreme degrees of cold continuously. Although this has been recommended by some authors in gonorrheal ophthalmia with the idea that a temperature unfavorable to the gonococcus could be maintained, the danger to the cornea seems to outweigh this theoretical advantage, and it is considered safer to use cold only for alternate one-hour periods.

The application of cotton frequently changed from a bowl of cracked ice to the closed lids is a method often employed and is much more efficient than the usual ice-bag. This method cannot be employed in the presence of a recent wound, however, as sterility cannot be observed. Cracked ice in a rubber glove applied over a thin layer of gauze is an efficient and clean method of applying cold.

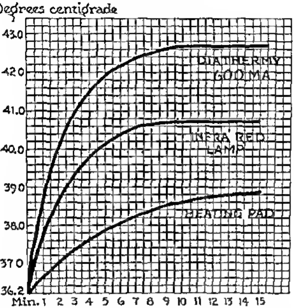

FIG 24.—Elevation of temperature in anterior chamber obtained by various methods (From Moncreiff, Coulter and Holmquest.)

In experimental work with accurate recording devices introduced into the tissues, Moncreiff, Coulter and Holmquest compared the elevation of temperature which could be produced by the electric heating pad, infra-red lamp and diathermy. All were applied for fifteen minutes with the maximum amount of energy tolerated by the skin. In the case of diathermy this was a current of 600 milliamperes.

The recording device was introduced in the conjunctival sac, anterior chamber, vitreous, and the apex of the orbit. In all these regions, the greatest elevation of temperature was produced by diathermy reaching 43.3° C. in the conjunctival sac, 42.8° C. in the anterior chamber, 43.2° C. in the vitreous and 40.9° C. in the orbit. Figures for the infra-red lamp were, 41.8° C. in the conjunctival sac, 40.7° C. in the anterior cham-

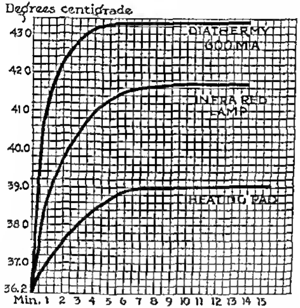

FIG 25 —Elevation of temperature in conjunctival sac obtained by various methods. (From Moncreiff Coulter and Holmquest.)

ber, 39.2° C. in the vitreous and 39.5° in the orbit. The rise of temperature produced by the heating pad was slight, reaching 39° C. in the conjunctival sac, 38.8° C. in the anterior chamber, 38.5° C. in the vitreous, and 37.5° C. in the orbit. Thus in all these locations, the rise of temperature produced by diathermy was 3° C. or more, and that produced by the infra-red lamp was 2° C. in excess of that produced by the

heating pad. (See Figs. 24 and 25.) No damage to the tissues was observed after such degrees of heat. These experimental observations confirm the clinical experience that *modern infra-red lamps offer a more efficient means of applying heat to the eye than ordinary sources of dry heat.* The method is clean, so that it is applicable to patients recently operated upon, and does not require the constant attendance of a nurse as does the proper application of moist heat.

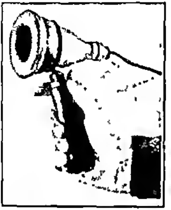

FIG 26 —Ophthalmic lamp of Park Lewis for infra-red treatment

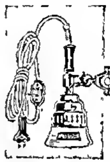

FIG 27.—Small infra-red lamp (Burdick) for applications to the eye and orbital region

Infra-red heat penetrates more deeply into the tissues if applied directly to the skin. The closed lids offer sufficient protection to the globe so that no gauze need be interposed between them and the lamp. It is practically impossible, without causing pain, to apply heat through the closed lids to a degree endangering the cornea, except in patients with impaired sensitivity of the fifth nerve. Patients acquire an increasing tolerance of the sensory nerves to heat, however, so that occasionally an unpleasant hyperemia of the skin or even desquamation may be produced by prolonged heat. This must be watched for when heat is used about the eyes.

A lamp especially adapted for ophthalmic patients has been devised by Park Lewis. (See Fig. 26.) It has proven

exceedingly convenient, as it heats only the eye and orbital contents. The small infra-red lamps such as that shown in Fig. 27 are equally efficient and avoid the smell of rubber, to which some patients object in the lamp previously mentioned. For use by the patient the ordinary bath-room heater with a coil and reflector is very useful and inexpensive. A form of heater which employs the heat generated by salts crystallizing after boiling has been adapted to ophthalmic conditions by Evans. After boiling the pad for four minutes, a temperature of 118°–120° F. is produced which lasts for one hour. This pad is always sterile when ready for use and may be used where no electric current is available. It may be used a great number of times without any decrease in the amount of heat produced.

MEDICAL DIATHERMY.

This term, as defined by Coulter describes "*the production of heat in the body tissues by high frequency currents, insufficient in amount, however, to produce temperatures high enough to destroy tissues or impair their vitality.*" These currents are applied by three methods. 1. What is known as *conventional diathermy* employs metal electrodes in contact with the body. The current is not of very high frequency, usually from 500,000 to 2,000,000 cycles per second. Since the amount of heat generated in the tissues by this method is inversely proportional to the size of the electrode, a large plate of tin is used as the indifferent electrode, placed upon a distant part, while a smaller plate, placed over the part to be heated, forms the active electrode. For ophthalmic purposes this is usually a metal cup fitted over the eye or orbital contents.

2. The second method is the use of a high-frequency electric field, employing a current of 10,000,000 to 100,000,000 cycles per second. The electrodes are not in contact with the skin, but the electrodes are insulated with rubber or felt

to prevent arcing from the metal to the skin. For this method the term *"short-wave diathermy"* is employed.

3. The third method is that in which an *electro-magnetic field* is set up in the tissues, the current being conducted by a flexible, heavily insulated cable which is wound about the part to be treated, a towel being interposed to prevent arcing. Various claims have been made for the superiority of short-wave diathermy or the method of electro-magnetic induction in certain conditions, but the summary of Coulter may be accepted as in accordance with what facts are available:

"1. The indications for short-wave diathermy are essentially the indications for conventional diathermy It may be shown later that the superior heating ability of certain high-frequency apparatus will be effective when conventional diathermy has failed. Further research and careful evaluation of clinical results are required.

"2. So far as competent investigators have been able to determine, there is no demonstrable selective thermal action *in vivo*, nor specific biologic or bactericidal action that may be attributed to short-wave diathermy. To date, the effects produced can be explained only on the basis of the generation of heat."

The indications for medical diathermy in diseases of the eye are by no means well established. One condition in which it has advantages is the occasional *orbital cellulitis* which does not localize well enough so that incision is effective. Here a large sheet of tin or aluminum is moulded to cover the region, this being used as the active electrode, the still larger indifferent electrode being beneath the patient. It must be remembered that the larger the active electrode, the less heat is generated at any point, so that this method avoids a degree of heat dangerous to the eye, provided that only 200 to 400 millamperes be employed, and that the current be reduced whenever the heat becomes uncomfortable to the patient. Treatments should begin with five to ten minutes and be increased to not over twenty-five minutes, being

repeated every two to three days. Marked relief of pain may result from such applications in the neuralgia of herpes zoster, and Monbrun and Casteran report good results in certain corneal ulcers, especially those following facial paralysis.

The author has reviewed the subject of short-wave diathermy up to 1938. It was shown that somewhat higher temperatures could be produced in the eye and orbit by this means than by conventional diathermy, without burns of the skin. Kokott raised the temperature in the vitreous of rabbits to 107.2° F. after ten minutes' treatment with the Siemens Ultratherm. Temperature in the orbit was considerably less. Puntenney and Osborne with similar technique produced temperatures of 107° to 109° F. in the vitreous, which dropped rapidly after treatment was terminated. They observed no dilatation of the visible retinal vessels such as had been claimed to occur by other observers. Varying clinical results have been reported, chiefly in the German literature, the report of Gutsch being especially enthusiastic about the method in chronic uveitis and vascular fundus diseases. Burki in a recent review reports results in 144 cases. Best results were observed in acute pyogenic infections. Burki is not convinced, however, of any marked superiority of the method over other methods of applying heat. It does not seem safe to raise the intraocular temperture above 105° to 106° F., and if this method of applying heat is employed, care must be taken to employ doses which will not exceed this and a technique which will not burn the superficial tissues. Further observations are necessary to establish the most effective dosage compatible with safety.

HYPERPYREXIA PRODUCED BY PHYSICAL MEANS.

Following the results of malarial inoculation in neurosyphilis, work by Neymann and Osborne and other investigators showed that hyperpyrexia produced by physical means had the same effect on this disease without the obvious disadvantages of malaria. Various means were employed to

maintain the body temperature at high levels for prolonged periods. The methods now most employed are the use of air-conditioned cabinets and that of electro-magnetic induction. In the former method, as described by Simpson and Krusen, the circulating air is heated and blown over the body, humidity and other factors being controlled. In the second method the body is placed in an electro-magnetic field, usually in some form of cabinet, the heat being generated by a high-frequency current. With this method the temperature can be raised rapidly, but accumulation of perspiration allows arcing of the current to the skin and must be prevented by various means. The combination of air-conditioning and electro-magnetic induction is employed in certain cabinets. Krusen has reviewed methods and the results obtained in various conditions (1935) while Simpson and Culler and Simpson (1936) have described especially the results obtained by use of the air-conditioned cabinet, including those in certain eye diseases.

Fever produced by physical means, in addition to effects similar to those of foreign protein shock, is apparently capable of killing certain organisms in the tissues by temperatures of 104° to 105° F. which are maintained from four to six hours. Such temperatures cannot be produced nor regulated safely by foreign protein or other parenteral therapy. Organisms especially susceptible to such temperatures are the Treponema pallida and the gonococcus, and hence it is in diseases due to these organisms that hyperpyrexia has been chiefly employed. Treatments, in spite of all possible care, are exceedingly unpleasant to the patients, and are not without risk of dangerous or even fatal reactions, chiefly the result of cardiac or circulatory collapse. Most clinicians require a careful physical examination, including electrocardiography, before undertaking treatment, and reject old and debilitated patients and those showing evidence of myocardial damage or marked hypertension. A trained technician must be in constant attendance during treatment under

direct supervision of the physician, which makes the treatment somewhat costly. For these reasons hyperpyrexia should be employed only in those ophthalmic diseases which involve serious danger to the sight, and which do not respond to less complicated and dangerous methods. The principal conditions answering these requirements are interstitial keratitis and luetic optic atrophy. Results in these conditions will be discussed on pages 272 and 337. In the more common types of ocular syphilis which yield to the usual antiluetic treatment, hyperpyrexia is seldom indicated. In gonococcal conjunctivitis of the adult, which once offered such a bad prognosis for survival of the cornea, excellent results were obtained by hyperpyrexia with rapid sterilization of the conjunctival sac and freedom from corneal involvement. At about the same time, however, results with the sulfonamides began to be reported which seemed to equal those of hyperpyrexia, secured with less discomfort and expense to the patient. The results of both methods will be discussed on page 224.

SURGICAL DIATHERMY.

This term describes the *production of heat in the tissues by high-frequency currents of such a degree as to cause destruction of tissue.* When the active electrode is of small size, such as that of a needle or small ball, such an amount of heat is generated by a suitable current. Aside from the application of the method in retinal detachment, which will not be discussed here, there are a number of ophthalmic conditions in which surgical diathermy may be employed conveniently and effectively. Details of technique are discussed in the handbook of Monbrun and Casteran.

The forms of apparatus commonly employed are not suitable for use in ophthalmology, where much weaker currents must be utilized. A special milliamperemeter recording currents *below 100 milliamperes is necessary. These authors* describe (Fig. 28) a special ebonite handle with applicators in

the shape of delicate needles, hooks and blunt instruments suitable for surgical diathermy about the eye, and a set of metal eye-cups fitting over the closed lids to be used for a more diffuse heat effect (medical diathermy). The lids are

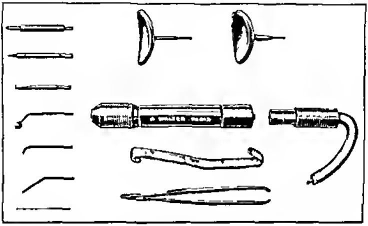

FIG 28.—Electrodes, holder and glass lid retractor for diathermy. (From Monbrun and Casteran, La Haute Fréquence en Ophthalmologie, courtesy of Masson & Co)

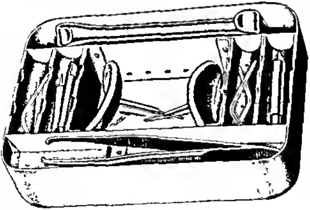

FIG. 29 —Diathermy apparatus in box for dry sterilization. (From Monbrun and Casteran, La Haute Fréquence en Ophthalmologie, courtesy of Masson & Co)

controlled by a glass lid-holder. While some such special equipment for ophthalmic work is necessary, this need be neither cumbersome nor expensive, and with the precautions mentioned above, certain procedures may apparently be carried out very conveniently and with perfect safety. (Fig. 29.) The apparatus devised by Walker for use in retinal

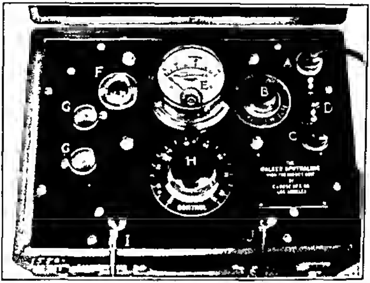

Fig 30.—The Walker ophthalmic high-frequency unit. *A*, main line; *B*, meter switch (low, high or out) 0-250 0-1000, *C*, foot switch, *D*, main switch, *E*, thermo-couple meter, detachable on jacks exposing replaceable protective fuse block, *F*, pilot light, *G*, fixed spark gap, *H*, choke rheostat controlling current to patient, *I*, micro puncture handle, *J*, indifferent electrode

detachment is also suitable for diathermy as usually employed about the eye. Current of low amperage is delivered and accurately measured with this apparatus. (See Fig. 30.)

One condition in which there is no doubt of the efficacy and convenience of diathermy is that of *trichiasis*, where a few lashes must be destroyed. The generally used method of electrolysis, while effective, requires that the current be continued thirty seconds for destruction of each lash follicle,

and in spite of careful local anesthesia, can seldom be accomplished without some pain of a very unpleasant kind, with a tendency for the patient to make involuntary jerking movements. Surgical diathermy requires only one second for the destruction of each lash, and after infiltration with novocaine the procedure is painless. A fine needle, used as the active electrode, is inserted in the lash follicle and a current of 150 milliamperes is applied for one to two seconds. The current is interrupted before the needle is removed, as otherwise a spark will be produced. If the lash resists gentle traction with forceps the coagulation has not been sufficient and should be repeated. A number of lashes may be removed in this way at a single sitting, but if more than six to eight inturned lashes are present, it will be more convenient to perform a plastic operation. The same method may be employed for the corneal portion of a pterygium but is more complicated than surgery.

Chalazion of the ordinary type is also more simply attacked by surgery, but where a small chalazion is present on the free lid-border, rather a delicate surgical procedure is required with the use of a stitch. Here diathermy presents distinct advantages because of the slow necrosis produced, with resulting delicate and practically invisible scar. The ordinary method is employed, with a large indifferent electrode under the patient, and a small needle as the active electrode. This is passed into the chalazion after infiltration and a current of 200 to 300 milliamperes is used for one second, this being repeated two or three times with the position of the needle slightly changed, according to the size of the chalazion. Small papillomata of the lids and lid-borders may be conveniently treated in the same manner.

Another use of surgical diathermy is the division of cicatricial bands of the orbit which prevent the wearing of an artificial eye. When these are divided surgically adhesions invariably occur, so that free grafts of skin or mucous membrane are necessary. On account of the delicate and nonretractile scars formed after electrocoagulation, it is claimed

that such bands may be simply coagulated with a needle-hook, using the same method with two electrodes. The bands should not be cut, but sufficient current and traction should be used to turn them white, two to three seconds at 200 to 300 milliamperes being usually sufficient. No sutures or dressings are necessary. A small temporary prosthesis may be worn immediately afterward and a permanent one made after fifteen days, when elimination of the necrotic tissue is complete. The same procedure may be used for neoplasms of the lids, using the electrode knife, with the advantage that a "barrage" can be made at the periphery by partial coagulation which will prevent the escape of tumor cells from the diseased area, the resulting scar being much smaller than where a zone of healthy tissue around the tumor is removed surgically.

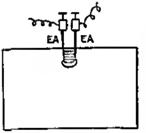

FIG 31 —Diagram of surgical diathermy with two active electrodes. (From Monbrun and Casteran, La Haute Fréquence en Ophthalmologie, courtesy of Masson & Co)

In *large tumors requiring evisceration of the orbit* surgical diathermy has long been used, because such coagulation blocks avenues of extension and may be performed with very little bleeding. For this purpose the use of two active electrodes is advantageous, the indifferent electrode being replaced by a branched handle carrying two small electrodes a short distance apart. (Fig. 31.) An intense heat is generated only in the zone between these two electrodes. This allows complete destruction of neoplastic tissue without danger of bony necrosis, which may occur after using radium, with which the zone of radiation cannot be so accurately localized. A current of slightly over 500 milliamperes is necessary. Monbrun and Casteran recommend that such large growths be destroyed in several sittings, and this possibility of dividing the operation without fear of causing extension is one of the great advantages of the

method, as after the slough has separated one can judge the necessity of further intervention.

It is regrettable that instruments for diathermy are not standardized so that a stated dosage will be the same with all instruments. On account of variations in voltage and other factors, the doses in milliamperes given above will have only a relative value, indicating to the physiotherapist a very weak or very strong coagulating effect desired, from which he must calculate dosage with the machine at his disposal. Fortunately *the immediate local effect of the electrode on the tissue furnishes the best evidence of the total dosage required.*

THE THERMOPHORE.

A device for the accurate application of ordinary heat to lesions of the eyes and adnexa is the thermophore, described about 1920 by Shahan. This is an electrically wired unit which may be adjusted to any desired temperature, with metal applicators to fit small lesions of various shapes and sizes. Post has recently summarized some of its uses, emphasizing especially its effect in deep infiltrations of the cornea which are not accessible to antiseptic agents. Here a temperature of 145° F. is applied for one minute. Small granulomata of the free lid-border, which are probably of the same nature as chalazia, yield readily to the same treatment, and xanthelasmata are sloughed off with a minimal scar following one or two such applications, he states. This instrument is not so widely used today, apparently, as it was soon after the perfected model appeared, and this is probably because the results in serpent ulcer, for which it was employed, proved disappointing.

ROENTGEN-RAY AND RADIUM.

In the use of roentgen-ray and radium precautions against harmful effects on the ocular structures are even more important than in the forms of physiotherapy previously discussed. The roentgen-rays penetrate the lids and cornea

and are absorbed in large part by the lens, where the resulting reaction has in a number of cases produced cataract. This has usually followed large doses given for carcinoma of the lids or for lupus. Stock reports such a case in which glaucoma also developed, following one irradiation of 110 per cent skin erythema dose, and another following repeated small doses. The author has seen two patients with cataract following rather intensive irradiation for lupus. A fairly large number of other cases was reported, and we now know that *small repeated doses have a cumulative effect, and that the lens changes may not appear for long periods after the irradiation, often not for one and a half to three years.* Individuals vary greatly in their susceptibility to roentgen-rays, which must be remembered in considering the absence of lens changes observed by Birch-Hirschfeld after intensive irradiation of animals, and the statement of Rados and Schinz that 150 per cent skin erythema dose was tolerated by the eye without reaction in their cases. Damage to the lids and cornea is also possible, the permanent loss of cilia being a not uncommon and sometimes necessary result of irradiation for carcinomata of the lids. Stock quotes, besides his own, several cases of glaucoma apparently resulting from roentgen-rays. He believes the total amount of roentgen irradiation should not exceed one erythema dose, unless the globe is protected. While a number of patients have undoubtedly received larger doses than this without developing cataract, there is certainly some risk in exceeding this dose, especially in children, since the growing crystalline lens is especially apt to develop cataract after irradiation. If more than this is required, the doses should be spaced over a period longer than one year. In certain malignant tumors it may be necessary to ignore the danger of cataract entirely and to give much larger doses. When the globe is protected, a subject which will be discussed later, doses may be given to the lids which will cause erythema and conjunctival inflammation. These reactions usually come on within six to ten

days of treatment and, if of the usual mild variety, subside within three weeks. Severe burns of the cornea occur rarely and may result in sloughing and perforation of the cornea. Such an accident should never occur, according to Cutler, unless the fundamental principles of dosage are violated. Injury of the retina is exceedingly rare, but has been reported. Irradiation of infants under two months may interfere radically with development of the entire eye.

Fig. 32.—Glass shell containing mercury for protection of the cornea during roentgen-ray and radium treatment (Made after Rohrschneider by Mager and Gougelmann)

Roentgenologists recognize that the measurement of irradiation in terms of the skin erythema dose is inexact, and many prefer the designation of dosage in *roentgen units* (R. U.). These units express the actual amount of radiation delivered at the distance of the lesion from the tube. This depends upon the current, filtration, distance and time employed. With the technique described on page 176, for

example, 100 roentgen units are delivered in fifty seconds. With this type of unfiltered irradiation, 100 R. U. equals approximately one-third erythema dose.

The harmful effects of overexposure of the eye to radium are practically the same as those produced by roentgen-rays. About the same number of cases of keratitis, cataract and glaucoma, most of which are mentioned by Kumer and Sallmann, have been reported after radium as after roentgen-ray treatment. The dosage which is tolerated is apparently, according to these authors, somewhat higher than that of roentgen-rays, 100 per cent skin erythema dose being about the upper limit of safety for one application and 300 per cent for the total dosage divided over a year. A most important factor in dosage, which it is often impossible to determine from reports of cases, is the amount of radiant energy delivered to the lens, the organ most susceptible to damage by irradiation. The radiant energy decreases very rapidly with distance from the source of energy, so that a plaque which delivers an erythema dose to the skin produces only a small fraction of this effect on the lens. Filtration also plays an important part in the dosage delivered. Individual sensitivity to radium also varies greatly, if one is to judge by reports of radium cataract in the literature. Larkin found that carefully calculated energy delivered to the lens varying from $1\frac{1}{2}$ to 5 erythema doses did not produce cataract in his cases. *It would seem safest, however, to keep the total dose received by the lens below three erythema doses.* In certain cases it is, of course, necessary to disregard possible damage to the lens in an effort to save life. According to Larkin, 50 mg. of radium screened with $\frac{1}{2}$ mm. of platinum applied for twenty-four hours delivers one erythema dose. In the treatment of malignant tumors applications must be so spaced that at least six skin erythema doses are delivered to every part of the tumor. In using implants of radium it may be estimated that 1 mg. for one hundred and twenty to one hundred and forty hours will destroy an area of malignant

tissue 1 cm. in diameter. In seeds of radon, the active emanation of radium, 2 millicuries of radon will destroy an area of tissue 3.5 mm. in radius. The effect of radon continues for approximately forty days, 50 per cent of its energy being used up in four days and 87 to 93 per cent in sixteen days. If the seeds are to be removed this is usually done after eight to ten days but in many cases the small gold capsules are left in the tissues. The lids must be considered especially

FIG. 33.—Wax prosthesis with lead filter for use of radium at 3 cm. distance. (From Kumer and Sallmann, courtesy of Julius Springer.)

sensitive to radium, 60 to 70 per cent of a skin dose being sufficient to produce an erythema of this region and a full skin dose often causing considerable damage. The lash-border must be kept out of the field where possible.

The previous discussion has related to the gamma or penetrating rays of radium which are present in preparations of the element and also in radon when prepared in the usual manner. It is these "hard" rays which are most important

in destroying malignant tissue, the soft alpha and beta rays being, as a rule, screened out by filters of various kinds. Woods has shown, however, that the *beta rays* are themselves useful in treating certain conditions. Because of their feeble penetration they do not reach the lens in significant quantities. The special indications for this method of irradiation are discussed on pages 183 and 189.

Protection of the Eye.—When treating the lids and palpebral conjunctiva it is *always possible and practically always advisable to afford some protection to the globe by means of some form of shell or prosthesis.* The roentgen-rays, as usually employed, are completely filtered out by 3 to 5 mm. of lead. Shields of lead were hence frequently employed to protect the globe. Unfortunately secondary rays are generated by this irradiated metal and these may produce burns of the adjacent structures. An article by Cutler and associates discusses the problems of protection. These authors favor the use of Wölfflin's prostheses, which consist of lead covered with thin layers of cadmium and nickel. The covering metals remove most of the secondary rays, so that the shells, which are only 1.3 mm. thick, afford more adequate protection against these rays than shields of lead. The protection against gamma rays, however, is practically the same as that of 1.3 mm. of lead and hence is not of great value when radium is employed. The shells are available in sets of three sizes. Oil or a bland ointment should be placed in the shell before they are applied, as otherwise they are difficult to remove. Another form of prosthesis has been described by Smithers. He employs a set of six contact glasses made of plastic resin covered with 1 mm. of lead. Cutler prefers the Wölfflin prostheses to the lead glass prosthesis filled with mercury which was advocated by Rohrschneider. (Fig. 32.) The latter, as well as Wölfflin's prosthesis, have been employed by the author in many cases receiving roentgen therapy, and have afforded adequate protection with the low dosages

employed. The prostheses of lead glass alone, formerly much employed, afford only slight protection.

It is more difficult in many ways to protect the globe against the gamma rays of radium. These penetrate 10 mm. of lead and hence the use of the shells just described removes only a small part of them, probably not over 20 per cent. The best protection is afforded by mounting the radioactive substance on pith or composition blocks of such a thickness as to remove it from the globe. (Fig. 33.) Such removal increases the size of the irradiated field and greatly lessens the amount of radiation reaching the lens. When interstitial irradiation of the lids with implants is employed, the amount of radiation reaching the lens from the small implants is seldom great. When treating tumors of the globe itself, protection of the lens is difficult and sometimes impossible. Some protection is afforded by windows in a thick lead shield which expose only the area to be treated.

Most details of dosage and treatment must be left to the judgment of specialists in irradiation therapy. The ophthalmologist should, however, be familiar enough with the principles of treatment to consult with the radiologist on individual cases which often present problems unfamiliar to the latter. It is necessary to insist on protection of the globe when referring patients to specialists who do not treat many ophthalmic cases.

The indications for roentgen and radium therapy will depend upon the site and extent of the lesion. In small neoplasms of the lids, when still free from adhesions to the bone, surgical excision with plastic closure of the defect will often be preferable to irradiation. *More diffuse neoplasms, especially such as are adherent to the bony orbit, present difficult or insoluble problems for surgery, while they may be satisfactorily cured by careful and thorough radiation.* (Figs. 34, 35 and 36.) The use of implants of radium or radon is convenient and effective in such cases, but probably involves more danger to the lens than roentgen therapy with proper protection of the globe.

For the *small precancerous or early cancerous hyperkeratoses* which are so common in older persons, the use of radium plaques is exceedingly effective. *Large orbital neoplasms* adherent to the orbital walls are often treated by evisceration of the orbit followed by radium or roentgen irradiation. Regaud and his associates have shown that previous surgery increases the danger of bony necrosis from subsequent irradiation and claim better results when no surgery has been attempted. Irradiation of such a large field requires large

FIG 34 —Angioma of inner canthus before and three months after treatment by curettage and radium. (From Kumer and Sallmann, courtesy of Julius Springer)

amounts of radium, and unless these are available, is better accomplished by modern roentgen equipment. In such treatment and in any irradiation about the face, protection of the other eye is exceedingly important.

Vascular nævi about the lids are especially suited to treatment with radium. This is especially true of capillary hemangiomata, in which the cosmetic result is usually far better than can be obtained with surgery, and often almost perfect. (Fig. 34.) The earlier these cases are treated, the more readily do they respond, since the young vessels are

especially sensitive to radium. *Nævus flammeus*, large blood cysts or hemangiomata supplied by large vessels do not yield so readily, and some of these are better treated surgically. *Xanthelasmata* are usually easy to remove surgically, with practically invisible scars, and it is only in the case of unusually large ones that radiation will be considered. *In spite of the favorable reports of many authors*, Kumer and Sallmann consider them as not especially adapted

Fig. 35.—Carcinoma of the lids before and three months after extirpation and radium treatment. (From Kumer and Sallmann, courtesy of Julius Springer.)

to radium therapy. *Detailed case reports, with indications* for and against roentgen and radium therapy will be found in the monographs of Kumer and Sallmann and of Stock and in the article of Regaud and associates, previously referred to.

Among the inflammatory ophthalmological conditions in which roentgen therapy is especially useful is *blepharitis of the more severe type* which has proven refractory to the usual methods. Here two or three roentgen-ray treatments will

often entirely relieve a condition of years' standing. A technique for which the author is indebted to Dr. James Case has proven effective in his patients and has produced no harmful effects. The rest of the lids being protected by leadfoil, the lid-borders are exposed to irradiation employing no filter, 3 milliamperes of current, 95 to 100 kilovolts at a distance of 8 inches for from forty seconds to one minute. This should deliver approximately 100 roentgen units. This is repeated weekly and usually three treatments are given. Other authors advise one-third of a skin dose as a routine for this condition. The lashes have never been lost, even temporarily, in these cases. The same method of treatment is used for cases of chronic dermatitis of the lids, and is equally effective. The smaller of these doses is usually sufficient for this condition.

The treatment of pituitary tumors is of especial interest to ophthalmologists, and here the question of irradiation often comes up. *The adenoma is the only form of pituitary tumor that is responsive to irradiation,* which is of no effect in the Rathke pouch type of tumor or cystic tumors and of little effect in meningiomata. Where these latter types can be ruled out a trial of irradiation may be made. In some cases such a trial may give diagnostic evidence as to the type of tumor, and in cases which refuse operation a trial of irradiation is indicated, unless a Rathke pouch tumor can be definitely diagnosed. *Roentgen therapy is usually the only method of irradiation to be considered,* since radium therapy cannot be directed to the site of the tumor without producing incalculable damage to the surrounding important structures. Only in the case of a tumor which has eroded the floor of the sella or where sellar decompression has been done may radium be used through the sphenoid region in addition to roentgen therapy.

The technique as employed by Dr. James Case depends upon the use of many small fields on the face and head through each of which a dose insufficient to cause epilation is directed accurately toward the pituitary body. It thus receives 30

per cent of the radiation applied to the skin in each area. The areas used by Dr. Case are as follows:

Mid-frontal, right and left temporal, nasal, through the open mouth, through the up-turned mental space, each cheek and certain areas of the scalp. The following factors are employed in each treatment:

Voltage	200
Filtration	1 mm copper
	1 mm aluminum
Intensity	5 milliamperes
Time	20 minutes
Energy delivered	200 roentgens

Treatments are repeated daily to different areas until all areas have been treated. One course to 12 areas should deliver 2400 roentgen units. The course may be repeated in the same order once or twice as indicated by clinical symptoms so that a total dosage of 7200 roentgen units may be delivered to the skin, about 35 per cent of which reaches the pituitary gland.

In the case of brain tumors which are inoperable and which are damaging the vision in spite of decompression a trial of deep roentgen therapy may be made, with the possibility that the tumor's growth may be checked or that the resulting atrophy of the choroidal plexus will diminish the pressure from an internal hydrocephalus. A scheme of treatment much like that described for treatment of pituitary tumors may be worked out if the approximate location of the tumor is known.

The use of roentgen therapy for intraocular inflammation, especially tuberculous iridocyclitis and choroiditis, must be considered as still in the experimental stage. Since the lens cannot be protected in such treatments there is always some danger of producing cataract, although this has been avoided in most cases by the use of small doses. Scheerer and Stock, after trying larger and smaller doses, settled upon 15 to 20 per cent erythema dose, repeated after seven weeks, as the

most effective dosage which could be safely used. The long interval is advisable, to avoid the secondary reaction which often occurs after four weeks. Stock advises no more than a total dosage of 60 per cent erythema dose in a year, divided into three or four applications. Stock and Scheerer, out of 38 cases, report some good results in very severe cases. The use of three-fourths erythema dose given during three weeks, as advised by Gilbert, according to Stock's experience, would seem to be too large, and with that of Braun and Herrenheiser,

A B

FIG 36.—Epithelioma of the conjunctiva. A, before treatment, B, after radium treatment. (Courtesy of Dr. William C. Bane.)

one-sixth to one-eighth skin dose, the interval of seven days is apparently not long enough to avoid a cumulative effect. These authors report 3 cases of tuberculous choroiditis treated with good results, but Stock has seen similar cases develop fresh lesions during treatment and considers the effect of the treatment in their cases as doubtful. While in the severe cases of tuberculous uveitis and sclerosing keratitis which have resisted other treatment a trial of small doses of roentgen-ray is apparently indicated, its use in ordinary iritis,

as advised by Horvath, is certainly not necessary, as other perfectly safe methods are usually effective in these cases.

In *beginning post-traumatic or postoperative intraocular infections* there is some evidence that roentgen irradiation may be of value. In these conditions, in which the fate of the eye is decided within a few days, the addition of 1 or 2 one-fourth erythema doses of unfiltered rays to the other measures employed has seemed in a few cases to turn the tide in favor of the patient. In other pyogenic infections, such as *early deep hordeolum* and *acute dacryocystitis*, a dramatic effect may sometimes be observed following one or two small roentgen irradiations. The mechanism of such beneficial effects is considered in a recent review by Desjardins. He is convinced of the value of roentgen therapy in many forms of infection, the most striking effects being observed in acute pyogenic infections when treated in the early infiltrative stage. In such conditions one or two very small doses, not over 25 per cent of a skin dose, are superior to larger doses, while in chronic inflammations somewhat larger doses are necessary. According to Desjardins the effect of irradiation depends chiefly on destruction of leucocytes, which are exceedingly radio-sensitive, in the tissues, with liberation of the protective substances contained in them. Following such destruction increased production of leucocytes occurs. Active hyperemia may also be a factor.

In *thrombosis of the central vein*, Lowenstein and Reis saw marked improvement in vision in 2 cases following divided doses of roentgen irradiation. Hessberg is also exceedingly enthusiastic about the method. He insists on the value of early treatment, giving 100 R. U. of hard rays followed at intervals of five to ten days by 3 to 4 doses of 50 R. U. The factors in his technique are: current, 180 kv.; filtration, 0.5 mm. copper and 3 mm. aluminum; distance, 40 cm. He believes a special advantage of such treatment is in preventing secondary glaucoma. The author has advised such treatment in a small number of cases. In branch thrombosis

clearing of hemorrhages occurred and vision improved, but this is known to occur spontaneously in many cases. In complete thrombosis no improvement of vision was observed.

A very definite indication for the use of radium exists in the condition of vernal conjunctivitis. A number of these cases are relieved of their symptoms by adrenalin, by intravenous injections of afenil or by desensitization to some specific protein. Others, however, are not so relieved, especially the cases with large flat papillæ of the upper lid, and these cases should he given an opportunity to try radium therapy, as many are relieved only by tbis means. The author has used the technique recommended by Dr. Laura Lane, of the Todd Memorial Institute, and in a small number of very obstinate cases has seen almost entire relief of symptoms, with disappearance of most, if not all, the papillæ and their replacement by smooth scar tissue. Radium is mucb to be preferred to roentgen-ray in these cases, the latter not having apparently the same effect on the condition. Loss of lasbes has not occurred when the following technique of Dr. Lane* was adhered to. That this technique is not entirely safe, however, has been proved by the occurrence of cataract in one and possibly two of the author's patients from five to ten years after treatment.

"In the palpebral form tbe following method of using radium in vernal conjunctivitis has proved effective.

"Fifteen to 20 mg. of element or the same number of millicuries of radon are used witb the following screening:

Platinum	0 05 mm.
Brass	1 00 "
Rubber	1 00 "

"This tube is placed at 1 cm. distance from the closed lids. A piece of Columbian paste or gauze is placed between the tube and lids to keep the radium at the proper distance.

"The duration of the exposure is from one-half to one hour, according to the age of the patient and the severity

* Personal communication.

of the disease as well as the amount of radium used. The first dose is usually only applied for one-half hour in order to judge somewhat the sensitivity of the patient.

"The sittiug is repeated after ten to fourteen days, according to the response obtained, the severity and the duration of the disease. Three to four such sittings are given. It is often necessary to lengthen the interval between sittings to three weeks.

"At the time of the above sittiog, in addition to the radium applied through the closed lid, a direct application to the everted lid is made. No screen is used other than the platinum. The amount of radium used is preferably a 15-mg. platinum needle. This is sterilized by placing it a few minutes in a 10 per cent formalin solution, followed by 70 per cent alcohol and then with sterile water and wiping off with sterile gauze. A few drops of a 1 per cent cocaine or hutyn solution may be used to make the everting of the lid less unpleasant.

"The needle is moved slowly across for three minutes, at 2 mm. distance.

"After the third or fourth application, according to the response aud the severity of the disease, a rest is given for two or more months. Then a similar series of treatments is repeated. The interval between these treatments is two weeks. In the more stubborn cases which have lasted for years, and in those cases subjected to much previous caustic treatment, it is well to give a third series some months later, particularly late in the winter.

"When the papillæ are very deose and cobblestone-like more time will be gained and a more satisfactory response obtained by anesthetizing the palpebral conjunctiva and snipping off or rolliog the papillæ, then applying a 5-mg. varnished applicator plaque, screened with 1 mm. of rubber, at 2 mm. distance, for three to five minutes at a sitting. Sittings are repeated at two-week intervals for three doses. It is often necessary to follow this series by one of irradiations

through the closed lids. The application of the platinum needle by the direct method may be used instead of the plaque, the exposures being slightly longer but not to exceed ten minutes. A needle plaque of 1- or 5-mg. needles can be used.

"**Hypertrophic Bulbar Form.**—In the hypertrophic bulbar form of vernal conjunctivitis the use of a 10- or 15-mg. platinum needle (0.05) for three to five minutes, at 2 mm. distance once in ten days for three doses is recommended. A second series of treatments may be given in a month, using in this series 1 mm. of rubber to screen the needle. The radium must be kept moving constantly above the area being treated so that an even distribution of the rays is obtained. Except in early cases, seen during the first year of the disease, screened applications through the lids will be necessary."

An important article has appeared by Quick, of the Memorial Institute, reporting the results in 82 cases of vernal catarrh treated by irradiation. His results were good, as 40 cases were apparently cured, 25 of these having been seen after one to nine years, and 32 were definitely improved. He recommends a technique quite different from Dr. Lane's, an "active deposit" of radium emanation collected on lead-foil, which is placed under the lids. Two hundred to 400 millicurie minutes are used for each eye in a treatment, and only a few such treatments at relatively short intervals are advised. Since the preparation of such "active deposit" is only possible in specially equipped institutions, he suggests the use of plaques of the element prepared to fit under the lids, with protective metal back and handle, the element being held in place by shellac, which gives slight filtration. He cautions against treatment through the lids, as involving danger to the lashes and as requiring the use of harder rays with the resulting danger of producing cataract, of which he has seen several examples. Local infections of the lid-borders must be cleared up, as irradiation in their presence is likely to be followed by corneal involvement. Repeated

doses over long periods are also dangerous, he believes. He concludes that *in spite of the good results obtained, on account of the dangers, especially to the lens, inherent in its use, radium should be reserved for cases in which all other methods have failed.*

Stallard employed in vernal conjunctivitis a spatula with a back 2 mm. thick made of an alloy of nickel and copper, holding on the front surface 7 mg. of radium salt unfiltered. This was slipped under each lid for an average of ten to twelve minutes. Treatments were repeated four to five times in seven to nine months in the cases which were cured.

The use of *beta-emanations* has been employed by Woods* and Moore in vernal conjunctivitis, with very encouraging results. They employ a radium tube containing 300 to 500 millicuries, which is held $\frac{1}{16}$ inch from the granulations for eight seconds. Treatments are given over long periods, once a week for three weeks and then once in three to four weeks.

In the case of **intraocular tumors**, glioma (retinocytoma) and sarcoma the hopes aroused during the early days of irradiation therapy have only in small part been fulfilled. Here, however, the danger of such treatment to an otherwise doomed eye need not be considered a contraindication, and since a few definite cures have been reported, irradiation must be considered in certain cases. Naturally, where only one eye is affected enucleation is still absolutely indicated. *It is only in bilateral glioma, especially where the second eye is much less involved, or in sarcoma of the only seeing eye, where enucleation is decided against by the patient, that irradiation should be undertaken.* In the case of glioma this should be preceded by enucleation of the first eye, unless both eyes are equally involved. Of a fair number of cases of glioma in which irradiation has been employed most have shown a temporary decrease in the tumor, followed by renewed growth and the usual fatal outcome. Of those treated by radium

* Personal communication

and mesothorium, Kumer and Sallmann record only one, that of Schönberg, in which a cure was obtained with vision of 2/20 after ten years, during which a cataract developed and was extracted. Schonberg used 144 millicurie hours followed in six months by 456 millicurie hours and again after two years by 3036 millicurie hours, with filtration for the use of gamma rays. To this case must be added that of Benedict, a child, aged four years, with a growth involving the retina from near the nerve forward almost to the orra serrata on one side. Six thousand milligram hours of radium were given, with treatments repeated after six months until 90,000 mg. hours had been given. The tumor disappeared, leaving only a flat scar and vision improved to 6/7. After five years lens opacities developed, reducing vision to 6/60, but there was no recurrence. The diagnosis of glioma was confirmed by sections of the enucleated first eye. While dosage must vary with individual cases, in general it may be said that gamma rays should be employed, and that the method of cross-fire irradiation, with the radio-active substance at 2 to 3 cm. from the eye, is to be preferred. One-fifth skin dose daily every second day for six to eight treatments is recommended by Kumer and Sallmann, with further treatments after two to three weeks as indicated by the result obtained.

In Stallard's monograph, which should be consulted for many details of treatment with radium, 5 cases of retinocytoma are reported which were treated by implantation of radon seeds in the tumor itself or suture of such seeds on the sclera overlying the tumor. One case was to all appearances healed after three years, with vision of 6/12, and another, still under treatment at the time of his report, was doing well. Seeds containing 3 millicuries of radon were placed directly in the tumor through a scleral incision, the attached thread being buried beneath the conjunctiva. After eight days the seeds were removed by the thread. For a neoplasm estimated at less than 4 mm. in radius, one 3 mc. seed should

be enough, while for larger growths more should be employed. The procedure may be repeated if the growth does not appear to be destroyed. No evidence was observed of neoplastic extension through the scleral openings, and for many reasons this seems the most logical method of applying radium in the rare cases in which this form of therapy is indicated.

Roentgen therapy for retinal glioma has been well reviewed by Martin and Reese. Including cases treated by roentgen and radium therapy, they could find only 2 cases in which healing was confirmed after five years and 3 after three years. The case of Verhoeff had vision of 20/30 after three years. To these may be added one of Scheyhing with vision of 6/10 after ten years. The amount of irradiation received in most of these cases was relatively small, too small, Martin and Reese, feel, to produce uniform results in a type of neoplasm which they find is rather resistant to irradiation. In 8 cases which they report, the Coutard method of multiple divided doses was employed. As modified by these authors, treatment consisted in a large total dose of deep roentgen irradiation applied in 50 to 75 divided doses over periods of twelve to twenty months. Such large doses, which amounted to 12,400 roentgen units in one case, were given with no serious damage to surrounding structures only by the employment of metal tubes 2.5 cm. in diameter, by which the radiation was limited to the desired area. The beam was accurately directed to the lesion and the direction of approach was changed at each treatment; nasal, temporal and anterioposterior fields being employed. (See Fig. 37.) Two hundred fifty to 400 roentgen units were given at each treatment and treatments were repeated two to three times a week. Moderate erythema and desquamation of the skin occurred regularly. When the conjunctival reaction, with photophobia and discomfort, became marked, treatment was stopped for a month. A current of 200 kv. and 30 milliamperes was employed, filtered with 0.5 mm. of copper and 2 mm. of aluminum, at a distance of 65 cm., the tube delivering

35 R. U. per minute. Results by this method were exceedingly encouraging.

Five patients are living and well with good vision after periods of seven, six, two and one-half, two years and three months following completion of treatment. Three other patients are living, but without useful vision. Five out of 6 cases treated for tumor tissue remaining in the orbit immediately after enucleation are living and well. No cases recovered, however, in which recurrence of the tumor in the orbit

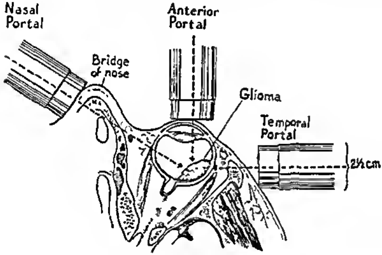

FIG. 37.—Technique of roentgen irradiation for retinocytoma. (From Martin and Reese)

had occurred. Martin and Reese feel that this method offers advantages over previously reported methods and that it has made irradiation the treatment of choice when glioma is present in the second eye after enucleation of the first. Wheeler suggested that irradiation might be preferred to enucleation when only one eye is involved if the neoplasm is still relatively small. When the tumor is large, however, the statement made on page 183 still holds, that eyes with unilateral glioma shall be enucleated and that irradiation

shall be reserved for involvement of the second eye. It is difficult to compare the results reported by Martin and Reese with those in patients treated by radon implants according to Moore and Stallard. More cures are reported by Martin and Reese. The two methods are apparently the only ones by which irradiation is allowed to reach an intraocular tumor in amounts sufficient to cause retrogression in a considerable proportion of cases. Both methods have certain advantages and disadvantages and later reports will be necessary to decide which is preferable.

Irradiation of the orbit after enucleation for glioma or melanosarcoma has long been practised by many ophthalmologists. *Where careful examination of the enucleated eye,* especially of frozen sections of the orbital end of the nerve in glioma *shows evidence of extension into the orbit* or past the cut end of the nerve, *irradiation is positively indicated,* usually after evisceration of the remaining contents of the orbit. Even where such examination shows no extension some believe it safest to irradiate as a precaution. The necessity of this is doubtful, however, especially in melanosarcoma, since clinical experience has shown the rarity of local recurrence in this condition. Von Hippel, who has studied the subject carefully, believes it is sufficient to enucleate in these cases, and Watzold, who formerly advised postoperative irradiation in every case, found that recurrences failed to appear even in some cases showing evidence of extension, so that he now joins in von Hippel's opinion. The prevention of metastases by this means is doubtful, as is the prevention of glioma of the second eye, and since the scar tissue resulting from irradiation often makes the wearing of a prosthesis impossible, one hesitates to advise its use without more definite evidence of additional safety afforded. Where extension has occurred, or where one is in doubt, intensive roentgen-ray or radium therapy should be given. Both methods have their advocates, and probably both methods should be used, radium needles or radon seeds being

introduced into the orbit, and roentgen-ray used in addition, which will allow the dose of radium to be kept small enough to avoid bony necrosis. Where evisceration has been done roentgen-ray alone is to be preferred to avoid this complication.

A condition which is especially sensitive to either roentgen-ray or radium therapy is that of *multiple lymphomata of the orbit.* These growths, which are usually symmetrical and form puffy swellings of all the lids, fairly melt away under the influence of either of these agents, and in case of doubt as to the diagnosis a trial of irradiation should be made.

Grenz Rays.—The "border" rays described by Bucky are between the ultra-violet and longer roentgen-rays in the spectrum. They are generated at a low voltage (10 kv.) in a special tube which permits their passage. While their wave-length is considerably greater than that of the beta rays of radium, being about 2 Angstrom units, their physical properties in many ways resemble those of the beta rays, showing very slight penetrating power through filters or tissues. All but 14 per cent, according to Bucky, are absorbed in 2 mm. of skin and subcutaneous tissue. Hence, while not adapted for neoplasms of appreciable depth, they have the advantage of relative safety in treating superficial lesions. The dosage employed is measured in terms of roentgen units, 300 R. U. usually producing a slight erythema. Krasso has reported good results in treating dendritic keratitis, rosacea keratitis, superficial corneal ulcers, blepharitis and sclerosing keratitis. Pfeiffer has recently reviewed the subject, reported experiments on the eyes of rabbits and given his results in treating 302 patients with various ocular diseases. He and his associates demonstrated an increase in local antibody formation following irradiation and a definitely beneficial effect on the course of experimental corneal ulcers. In treating patients, 452 R. U. filtered with 0.024 mm. of aluminum was given twice a week for five treatments. Such courses were repeated in some cases four or five times with free inter-

vals of two weeks. Best results were observed in ulcers and infiltrates of the cornea. In catarrhal and marginal ulcers healing was usually prompt, as was the case with trachomatous ulcers. Apparently only one serpent ulcer was treated, but without effect. In dendritic keratitis and superficial punctate keratitis, surprisingly enough, results were not constant and could not be considered definite. In episcleritis and scleritis, results were considered good in 80 per cent New-formed corneal vessels decreased in size under treatment, but old corneal scars were not benefited. Dystrophic corneal conditions were not benefited. Definite relief of pain was noted by most patients, even when no objective improvement could be observed. The treatment was abandoned in conditions of the lids because of resulting pigmentation of the skin, and it was not attempted in conjunctival conditions because of the difficulty of exposure. Neoplasms of the lids and conjunctiva were not treated in this series. Aside from pigmentation of the skin and moderate conjunctival and scleral reaction in 2 cases, no undesirable effects of treatment were observed.

It may be concluded that a definite field exists for the use of the Grenz rays and beta emanations where facilities for their use exist. The field for both methods is similar, and includes superficial inflammatory conditions of the anterior segment, especially of the sclera and cornea. The penetration of these rays, which is greater than that of the ultraviolet and less than that of other forms of irradiation would seem to fulfil every theoretical requirement for irradiation under these conditions. Their relative safety permits a trial of their efficacy in a number of conditions which do not respond to other forms of therapy.

Beta Emanations.—Woods has reported on the use of this form of radiation in *tuberculosis of the anterior segment.* The gas from 1 gm. of radium is enclosed in a soda glass container, which is surrounded by a brass tube with a 4 mm. opening at one end. Such a preparation emits chiefly beta

rays which penetrate the tissues only 2 mm. and hence cause no damage to the lens or deeper structures. A small amount of gamma rays is also emitted, but this is so small that 60 per cent of an erythema dose of beta rays may be given with only 2 per cent erythema dose of gamma rays. Hence, if desired, 30 erythema doses of beta rays could be given without exposing the lens to more than 1 erythema dose of gamma rays. The tube is held almost in contact with the affected cornea or sclera during the very brief treatments. Twelve seconds with this technique gives 60 per cent erythema dose, which may be repeated in two weeks. Five seconds gives 25 per cent erythema dose and in certain cases this smaller dosage was preferred, being repeated once a week. A total of thirty-five to forty seconds, or 175 to 200 per cent erythema dose, is given over a period of four to six weeks in one course, which is repeated several times if indicated. In Woods' series 10 cases of tuberculous kerato-iritis healed after one course. Two of these cases had recurrences which healed on further courses. Three cases of severe deep scleritis were treated. One healed after eight months of treatment, 1 after two years, while 1 relapsed after one course and received no further treatment. During treatment corneal scars showed definite evidence of clearing, with marked improvement in vision. Such clearing showed a tendency to relapse when treatment was stopped, but further clearing occurred during later courses, the final results showing considerable improvement. Woods explains the effect as probably due to local mobilization of antibodies in the irradiated tissues. The author has watched one severe case of sclero-keratitis given such treatment by Dr. H. E. Davis with healing of all active inflammation and no recurrence during one year.

MASSAGE.

Massage is used chiefly in treating three conditions. *In corneal ulcer the clearing of the corneal scar is probably hastened and promoted by gentle massage* of the eye-ball with a finger

held over the closed lids. Two per cent yellow oxide of mercury ointment is usually used in the conjunctival sac for lubrication and as a mild irritant. The finger moves the lid back and forth over the cornea, such massage being kept up for five minutes three times a day. (Fig. 38.)

In glaucoma it is sometimes possible to keep the tension down to normal, especially after a filtering operation which does not produce quite enough effect, *by massage.* This

Fig 38.—Massage of cornea to aid clearing of corneal scar

forces fluid out of the eye, either through its normal channels or through a small wound in the sclera made at operation, in which case it collects under the conjunctiva to form a small bleb. Such massage should be performed with the two forefingers which hold the eye between them beneath the lids, and are alternately pressed in and released so as to slightly indent the globe. Just enough pressure should be used so that no pain is caused. Pressure is made and released about thirty times, and this is repeated two or three times a day. (Fig. 39.)

In *chronic infections of the Meibomian glands* fluid accumulates in their ducts, and the result is recurrent chalazion

FIG 39.—Massage of globe to reduce intraocular tension.

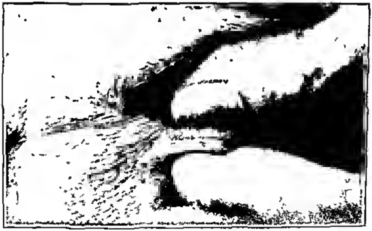

FIG. 40.—Massage of lids to empty Meibomian glands.

or a diffuse thickening of the lids. Chalazia may often be prevented and the infection helped considerably by massage of the lids. This is done, as shown in Fig. 40, by pressing,

with the two thumb-nails on the skin side of the two lids which are held together and away from the globe. Pressure should include the whole lid-border and should be continued until fluid ceases to come from the ducts of the glands at the lid-border. Another method is the use of a glass rod on the conjunctival side of the lid, which presses against a finger held on the skin side.

After having reviewed the uses of various forms of phototherapy, the following résumé of common ocular conditions in which physiotherapy is employed, with the form of treatment considered best for each condition, may help to clarify the material and facilitate its use in practice. To avoid repetition the reader is referred to the preceding text for the details of technique.

Diseases of the Lids.

Hordeolum: Moist heat, incision.

Chalazion: Incision and curettage. Electrocoagulation if on the lid border, 200 to 300 milliamperes for one second.

Xanthelasma: Surgery is simplest in most cases. Thermophore may be effective. Radium is effective but requires care.

Blepharitis: A trial of ointments and moist heat should be made. In resistant cases roentgen-ray is most effective.

Trichiasis: Electrocoagulation. 150 milliamperes for one second. If more than five or six lashes are affected surgery is simpler.

Dermatitis: Roentgen-ray is effective in small dosage.

Carcinoma: Surgery for small growths not adherent to the bone. Roentgen-ray where large areas of skin are involved. Radium for growth at lid-border or in the inner or outer angle, with adhesion to bone.

Nævus flammeus, hemangioma: Radium, especially for capillary hemangioma. Surgery for hemangioma supplied with large vessels.

Diseases of the Orbit.

Cellulitis: First twenty-four hours, cold packs. After this moist heat and incision. Medical diathermy, 200 to 400 milliamperes for five to ten minutes, may be tried.

Carcinoma: Radium needles or tubes of radon imbedded in growth. Where orbit is to be eviscerated electrocoagulation (surgical diathermy).

Sarcoma: Electrocoagulation for evisceration of the orbit.

Lymphoma. Radium in plaques over the lids. Roentgen-ray may also be used, but is not so effective.

Diseases of the Conjunctiva.

Acute conjunctivitis: First twenty-four hours, cold packs. After this moist or dry heat.

Chronic meibomitis: Massage of the lids.

Vernal conjunctivitis: Adrenalin locally and calcium systematically should be tried first. Where symptoms are not relieved, radium.

Neoplasms of the bulbar conjunctiva: Surgery. Electrocoagulation may be useful if a weak current and a needle electrode are used. Radium is dangerous bere.

Diseases of the Cornea.

Serpent ulcer: Local applications, atropine, keratotomy. In early ulcer phototherapy may be tried, using the carbon arc with uviol filter, or Grenz-rays.

Herpetic keratitis (dendritic ulcer): Phototherapy, using carbon arc with uviol filter eight to ten minutes once a day. Roentgen-ray, 30 per cent erythema dose (one to two treatments).

Epithelial dystrophy: Dionin. Phototherapy may be tried.

Degenerated corneal scar with ulceration: Phototherapy as for herpetic keratitis, or Grenz-rays.

Sclerosing keratitis: Phototherapy, using carbon arc with uviol filter ten minutes every two days. Roentgen-ray, 15 to 20 per cent erythema dose, repeated after seven weeks, no more than three or four treatments being given. Beta emanations or Grenz-rays may be superior.

Carcinoma: Surgery is usually best, followed by careful use of electrocautery. Where the sclera or interior of the eye are involved enucleation must be advised. If this is refused radium may be tried.

Phlyctenular keratitis and keratoconjunctivitis: General treatment and atropine. The use of sun-bath or general irradiation with the carbon arc or mercury vapor arc is of definite value in addition to other treatment.

Corneal scars: Massage of the cornea and the use of dionin are probably of as much value as anything in helping to clear scars. The use of ioatophoresis has been advised, but its value is questionable.

Diseases of the Iris and Ciliary Body.

Tuberculous iritis: General treatment and atropine are most important. Roentgen-ray as described for sclerosing keratitis may be tried, but is not without danger of causing cataract. Hence it is contraindicated in the ordinary forms of iritis and other diseases of the iris and ciliary body.

Diseases of the Choroid.

No form of local physiotherapy is probably effective. In tuberculous choroiditis the use of sun-baths or generalized light-baths with the carbon or mercury vapor arc may be of value.

Diseases of the Retina.

Glioma retinæ (retinocytoma): Enucleation of the first eye, followed by radium in the orbit, if there is recurrence. If the second eye is involved a choice may be offered between enucleation and roentgen-ray or radium.

Diseases of the Optic Nerve.

General fever therapy has given some good results, especially the use of the air-conditioned cabinet and diathermy.

Intracranial Diseases.

Pituitary tumor: If an adenoma is considered probable roentgenotherapy may be tried, large doses being directed to the sellar region through a number of fields. (See p. 176.) Where vision fails in spite of one or more treatments no time should be lost in advising surgery. Radium is only used where the tumor has eroded the floor of the sella, or after sellar decompression has been done.

Cerebral tumors: When tumor is inoperable or has been only partially removed decompression should be performed if the vision is being damaged. Deep roentgenotherapy may then be tried.

Glaucoma: Not amenable to physical therapy, except for the relief of pain by heat or cold and the use of massage for promoting filtration.

Roentgen-ray and radium are contraindicated in the presence of glaucoma.

Cataract: No form of physical therapy is indicated. The danger of producing cataract is one of the chief reasons for avoiding the use of radium and roentgen-ray except where it is necessary and for the careful protection of the globe when this is possible.

Diseases of the Muscles.

For the indications for muscle exercises see page 358.

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CHAPTER VI.

DISEASES OF THE LIDS.

HORDEOLUM.

THIS is *an acute infection of the glands of Moll or Zeiss, usually with Staphylococcus aureus.* Acute Meibomian styes are of the same nature, except that some of them result in permanent occlusion of one or more Meibomian ducts which leads to chalazion. In the acute stage their treatment is usually the same as that of hordeola. The cause of styes is apparently the closure of a duct with the inclusion of organisms in the glandular alveoli. In some cases apparently organisms of unusual virulence find their way into the gland wall and multiply or a patient's resistance is temporarily lowered so as to allow invasion of the gland wall by organisms ordinarily living as harmless saprophytes within its lumen.

When a case appears for treatment it must be decided whether the stye is ready to be opened. If only induration and redness are present it is usually best to postpone incision for one or two days. The frequent use of moist hot packs or the infra-red lamp will reduce swelling and hasten the natural process of "pointing." A certain number of styes may be aborted by such treatment, so as not to require incision. In the large angular styes, where so much swelling is often present that the first signs of abscess formation are difficult to see, the use of magnesium sulphate in saturated solution seems to reduce swelling more than heat alone. It should be applied on cotton which is protected from drying by rubber dam, such a pack heing left on for one hour three or four times a day. *When the slightest yellowish area near the lid-border can be seen incision with a very sharp cataract knife is indicated.* Often a yellowish point may not be seen, but a certain tenseness of the skin with the faintest perceptible gray area under it will point to the proper site for incision.

This should be followed by gentle pressure, as the pus may be too viscid to escape without this. While most styes are opened easily without anesthesia, certain larger ones, especially near the angles, cannot be opened without severe pain, and in such cases very careful infiltration with 4 per cent novocaine, the injection being begun well away from the site of the abscess, will allow incision to be made painlessly. If some of the solution is injected deeply, beneath the orbicularis, and an interval of five minutes is allowed, the severe blepharospasm always present will relax so as to allow access to deep angular styes which were inverted beneath the swollen lid-border. In a few high-strung patients either such infiltration or a few whiffs of nitrous oxide are required before the stye can be opened, and a prompt decision to use such procedures as soon as one is reasonably sure that pus is present will save the patient several days of acute discomfort.

When the infection has its origin in a Meibomian gland the same mode of treatment is indicated, with a few minor variations. Incision is usually best made from the conjunctival side, and may be made much less painful by touching the area to be incised several times with a small tooth-pick applicator soaked with 10 per cent cocaine or 2 per cent butyn. Sometimes pressure on the two everted lids between the thumbnails (Fig. 40) will evacuate pus through the duct, and if this is repeated after twenty-four hours incision may not be necessary. In some cases with a subacute Meibomian infection pus is not formed, and a hard nodule develops which must be opened and curetted as for a chalazion, after waiting for the inflammatory symptoms to subside.

After any hordeolum or Meibomian stye has been incised, even if no blepharitis is present, it is well to prescribe a 2 per cent yellow oxide of mercury ointment to prevent the infection of other glands. This should be continued for a month or longer. If the infection is Meibomian, and fluid can be expressed from other glands, massage once or twice a week is indicated to prevent further abscess formation.

In spite of such treatment, recurrences are common and demand other measures. Just how a refractive error may be responsible for such infections is not known, but it is supposed that the resulting blepharospasm, even if not so marked as to be noticeable, may occlude the mouths of the glands and allow bacteria to multiply in their ducts and alveoli. At any rate it is known that after careful refraction under cycloplegia, with the correction of rather small degrees of astigmatism or hyperopia such recurrences will often stop. This, with the use of one of the antiseptics, such as yellow oxide of mercury, is the first thing to be tried. If the patient is obviously anemic, or recovering from a general infection, as is often the case, cod-liver oil should be given, and here the newer preparations of vitamin A offer in some cases a welcome substitute for the cod-liver oil itself. (See Chapter III.) Iron may be necessary if true anemia is present, but this should usually be determined by the internist, and it is being recognized that iron is not so often necessary as was formerly believed. Attention to diseased tonsils, adenoids and sinuses will often give the first relief in these patients whose repeated hordeola have become a serious cause of disability.

This is one ocular condition in which an autogenous vaccine may play an important therapeutic rôle. A liberal amount of pus obtained on a sterile loop as it comes out after incision is spread on a blood-agar slant or plate or on Loeffler's medium, and incubated at once. A vaccine prepared from this by the technique of any good clinical laboratory and preserved in a vaccine ampoule is given subcutaneously in ascending doses, beginning with 0.1 cc. Injections should be made twice a week, the dose being increased 0.1 cc. each time, and fifteen to twenty injections are usually given. Naturally local treatment and cod-liver oil should not be neglected during this time. Some favorable reports have been made on the use of Besredka's antivirus in this condition. This is a filtrate of broth in which the offending organism has

been allowed to grow for ten days, and is supposed to contain substances which inhibit further growth of that organism. It is applied locally to the lid-borders on moist dressings. In a condition so variable as this, and in which spontaneous cure often occurs, reports of results are apt to be inconclusive, and the whole theory on which the treatment is based is by no means accepted. (See Chapter IV.)

BLEPHARITIS.

Blepharitis is in its nature similar to, and often associated with, hordeolum. *It is an infection of the lash follicles, usually with the staphylococcus,* the principal symptoms of which are redness of the lid-borders and the formation of scales consisting of dead epithelium and dried serous exudate. Small abscesses may be present around the cilia, showing as tiny circular ulcers. Often a chronic conjunctivitis develops when the blepharitis is of long standing, with thickening of the lower lid and follicle formation, and occasionally small marginal ulcers of the cornea may occur, after an acute exacerbation of conjunctivitis. There seems reason to believe that the chronic conjunctivitis is due to irritation from the constant presence of staphylococci and epithelia débris in the conjunctival sac, and that the acute exacerbations may be explained by occasional larger "showers" of such material acting on a sensitized conjunctiva. Some experimental evidence in this direction was afforded by Riehm, who showed that the conjunctiva could be sensitized by instillations of staphylococci and their products so as to react upon further instillations with conjunctivitis and the formation of lesions at the limbus resembling phlyctenules.

The ordinary case of blepharitis responds well to local treatment, the use of *2 per cent yellow oxide ointment* or *3 per cent ointment of ammoniated mercury,* twice a day, preceded by hot packs. Some patients respond to the first few applications with an exacerbation of their conjunctivitis,

apparently because of the débris from the lid-border which is rubbed into the conjunctival sac, and patients should be warned of this possibility. The author has seen a number of patients with blepharitis who showed increased symptoms of irritation after any of the usual ointments made up in a petrolatum base. Apparently petrolatum itself acts as an irritant in such cases, as substitution of an ointment made in pure lanolin has given relief in many such cases. A 2 per cent ointment of zinc oxide in lanolin or aquaphor has proven especially useful. Conjunctivitis, when present, should be treated by a weak zinc collyrium, and treatment should be continued for at least a month after symptoms have subsided. *When much scale formation is present the medication cannot reach the site of infection until these are removed.* This should be done very carefully one or two times by the surgeon himself, and often the cautious use of benzine on an applicator is an aid in this, allowing the ointment to penetrate well into the lash follicles afterwards. After removal of the scales an application of 4 per cent silver nitrate carefully limited to the lid-border is often of great value, and this may have to be repeated twice a week for one or two weeks. Medvedeff and Euffa have reported excellent results by the use of a *2 per cent solution of brilliant green in 70 per cent alcohol.* After thorough cleansing of the lid-border with benzine the solution is painted on with an applicator and allowed to dry. The startling discoloration remains for several days, and is a contraindication to such treatment in many cases. The author has seen good temporary results from this method in a few cases, but the condition tends to recur unless followed by other treatment. Where much itching is present the use of 1 per cent phenol or 1 per cent resorcin ointment often affords much relief, and the latter ointment may succeed where yellow oxide is without effect. The fact that certain persons are sensitive to resorcin, and develop a dermatitis after its use, should be kept in mind.

Where the conjunctiva is much inflamed the use of zinc solutions may prove irritating and here a collyrium of novocaine, 2 grains; adrenalin, 1 to 1000, 2 drams; boric acid crystals, 40 grains to 1 ounce of water, may prove most satisfactory, as it is cleansing, non-irritating and has a slight anesthetic effect. The use of staphylococcic toxid in blepharitis accompanied by conjunctivitis is discussed on pages 130 and 235.

As in recurrent hordeola, refractive errors and the general condition are important in blepharitis, and should receive the same treatment where local measures fail to procure relief. The continuance of blepharitis leads to its ulcerative form and to a condition called *epilating conjunctivitis*, in which many or all of the cilia are destroyed. Such a condition, besides its unfortunate effect on the patient's appearance, is a source of continuous discomfort and sometimes makes any continued use of the eyes impossible. In such serious cases local applications are often of no effect, and here *the use of the roentgen-rays has proven to be of inestimable value.*

Roentgen-ray treatments must be given with caution, to avoid a permanent loss of cilia or harmful effects on the deeper structures, especially the lens. It must be remembered that the epilating dose is, under certain circumstances, less than the erythema dose, and that individual doses and divided doses close enough together for a cumulative effect (two weeks) must be kept below this. In rare cases only a dose large enough to cause epilation will relieve the blepharitis, but this is seldom necessary (see Chapter V). When any roentgen-ray treatments are to be given to the lids *the only way to avoid possible damage to the lens is the use of a protective shell which is placed over the cornea beneath the lids.* (See page 172.)

A cause of failure in certain cases, according to Lincsz, is the inexact classification of cases before treatment is begun. He distinguishes sharply between *blepharitis ciliaris* of young adults and *seborrhœa* of the lid borders in older persons. The

former responds to treatment with noviform and mercury, while in the latter ointments or pastes containing bismuth subnitrate are preferred. Involvement of the lid border in *acne rosacea* yields more promptly to icthyol. Lincsz tries to distinguish between skins with an excess of oily secretions and dry skins. In the former the crusts should be removed with benzine and lotions containing zinc oxide and magnesium carbonate are preferred to oily preparations. In blepharitis affecting persons with a dry skin the crusts are removed by olive oil or purified cod-liver oil and ointments or oily pastes are used in treatment. In seborrhœa of the lid border, as well as in some cases of dermatitis, the author has found the stimulating properties of ichthyol and naftalan to be of value, and has employed the following prescription:

Naftalan	2 0 grams
Ichthyol	0 6 "
Zinc oxide } āā Starch }	7 9 "
Aquaphor qs	30 0 "

The use of aquaphor, a combination of cholesterol derivatives and wax, as a base for this and other medicaments is often preferable to that of petrolatum, as it is soft and is absorbed rapidly by the skin so that the pores are not obstructed as is the case when petrolatum is employed. It is also, like lanolin, miscible with water and with various substances in watery solution.

It must be remembered that a certain number of cases of blepharitis are due to the presence of fungi or yeast on the lid-border. Cases which do not react well to ordinary treatment should be carefully examined for these organisms, as if they are present treatment which is more definitely fungicidal will be necessary. This includes the use of 1 per cent resorcin ointment, sulphur ointment and painting the lash-border very carefully with one-half strength tincture of iodine or brilliant green (2 per cent in 70 per cent alcohol).

Roentgenotherapy, in combination with such treatment, seems to be as useful in these cases as in ordinary blepharitis.

INFECTIONS OF THE MEIBOMIAN GLANDS.

A not uncommon condition is that of chronic infection of the Meibomian glands, or chronic hypersecretion of these glands. Elschnig was one of the first to call attention to this condition, the author has emphasized its importance as the etiological factor in many cases of chronic conjunctivitis, and Filatow has recently shown that it may be responsible for certain forms of keratitis, especially after trachoma. He thinks it likely that broken-down products of the fatty secretion are responsible for the corneal and conjunctival irritation, while it seems as probable that the growth of bacteria

FIG 41 —Case of extreme hypersecretion of Meibomian glands

in these glands and the resulting bacterial products are at least equally irritating The condition is evidenced chiefly by thickening of the lids and by the presence of a foamy material in the conjunctival sac. *Pressure on the two lids expresses a yellowish material, sometimes clear and oily, but often flocculent and almost purulent. The treatment of this condition is by massage,* either through the everted lids (Fig. 40) or, as Elschnig recommends, by a glass rod on the conjunctival side pressed against a finger on the skin side. Such massage must be continued for a period of weeks and months, and often it is necessary to instruct a member of the family or a local physician in its use. Pressure must extend along

the whole lid-border and from the upper ends of the gland to their mouths and should be continued as long as abnormal secretion may be expressed. This treatment is combined with the use of an ointment to keep open the ducts of the glands, and for this a zinc oxide ointment in a waxy base is useful. A few cases have resisted such treatment, as well as all other forms of general and local medication, including autogenous vaccines. Roentgen therapy is worthy of trial in the most obstinate cases. It requires slightly heavier dosage than that used for blepharitis and the globe should be protected in the same way.

Chronic infection of the Meibomian glands is often the cause of multiple chalazia. Apparently the inflammation closes the ducts of a number of glands, and the retained secretion in each gland acts as an irritant to promote the formation of a granuloma. Such chalazia usually begin with signs of subacute inflammation, without the formation of demonstrable pus. They may often be prevented by massage of the glands and a zinc oxide ointment. When formed, they must be taken care of in the same way as any chalazion, and this is best done by incision on the conjunctival side, parallel to the length of the gland, and thorough currettage with a sharp spoon. Such curettage requires careful infiltration with 4 per cent novocaine and the use of a chalazion clamp which surrounds and fixes the nodule. (See Fig. 3.) When chalazia are at the lid-border the use of electrocoagulation is often preferable to incision, which in this location requires closure by sutures. After infiltration with novocaine a small ball-pointed electrode is inserted directly into the chalazion, or if its wall is not soft enough, through a small puncture wound, and a current of 500 milliamperes is used for two seconds, or long enough to turn the site of the nodule gray. Such small granulomata usually shrink up in the week following this procedure, without sloughing, leaving a smooth lid-border.

CONCRETIONS OF THE MEIBOMIAN GLANDS.

In certain persons, calcium is deposited in some of the alveoli of these glands, resulting in the formation of concretions. While these are covered by conjunctiva they cause no *symptoms*, but *as they become larger, the conjunctival* covering is worn through, and *irritation of the underlying cornea or bulbar conjunctiva results*. They are simply removed, after instillation of a local anesthetic, by the point of a cataract knife. They *may be very numerous, requiring several* sittings before all are removed. There seems to be no method by which their recurrence can be prevented, although massage of the lids as described above may be of some value.

DERMATITIS.

Contact Dermatitis.—An article by Hollander and Baer discusses in a very practical way this rather common condition. The skin of the lids is unusually thin and is constantly exposed to moisture from the conjunctival sac. Hence *it is likely to show inflammatory changes from contact with a large group of chemical substances which effect the rest of the skin very slightly or not at all.* Some of these substances are such as will produce chemical irritation on the skin of any person; others do so only in persons with an inherited or acquired allergy to such substances. The most common offenders in the former class are *cosmetics, especially orris root*, which is used in nearly all face powders; hair dyes, hair tonics and solutions used in curling or fixing a wave. Mascara is a rare cause of dermatitis. Substances used to dye the lashes have caused very severe dermatitis, especially one preparation called Lash-Lure. *Substances not used on the face may reach the lids through the common habit of rubbing the eyes*, and, especially from the hair, by means of pillow-covers. Many other substances cause dermatitis only in certain sensitized persons or after

prolonged use. Such are perfumes or oils used in various face creams or soaps; plants which give off a volatile oil such as the English ivy, geranium and primrose; and drugs which are used in the nose or eyes. Atropine, eserine, ephedrin, and various local anesthetics such as novocaine, butyn and pantocain are the commonest offenders in this group. Other drugs such as phenobarbital, and certain foods cause dermatitis when ingested, but usually in this case other parts of the body are affected. Some of the metals, such as nickel and gold, produce a characteristic dermatitis in the wearers of spectacles, while ointments containing mercury do so in certain persons.

When a patient complains of itching lids, and a slight redness of the lids, with a fine, dry, bran-like deposit of desquamated cells is present, chemical or allergic dermatitis should be at once considered and a search for the most likely cause should be instituted. Most severe cases will be diagnosed without difficulty. A careful history will often reveal the use of one of the substances likely to cause dermatitis, or of sensitization to one or more allergens. If the history is negative a number of possible causes may be eliminated by the prohibition of all cosmetics, including hair dyes and tonics, and the use of a non-allergic face powder, which contains no orris-root. A shampoo and covering of the hair at night, with a change of pillow-cases, is usually advisable. *Removal of the cause will be followed by complete relief in four to seven days.* Soap and water should be kept from the face during this time, a simple official cold cream being used for cleansing, followed at night by a calamine-zinc oxide lotion or the use of pure zinc oxide as a dusting powder. If conjunctivitis is present, as is often the case, symptoms of irritation are aided by a mild wash containing epinephrin in 1 to 4000 concentration. When relief is obtained restoration of certain ordinarily harmless cosmetics may be allowed, one at a time, *until the offending substance is discovered by a recurrence of* symptoms, when it is eliminated permanently.

Seborrhœic Dermatitis.—This condition *usually involves the lids from the affected eye-brows or scalp.* The affected area has a sharply outlined border, is covered with scales and itches intensely. It is best treated with *0.5 to 1 per cent sulphur ointment,* the strength of which may be increased slightly unless symptoms of increased irritation occur, when it should be stopped. Roentgen-ray therapy with one-fourth skin dose repeated four to six times at one week intervals is usually effective in cases refractory to sulphur. The globe should be protected by a shell of the type described in Chapter V.

Neurodermatitis.—This usually affects other portions of the body, but sometimes the lids alone are involved. It occurs in persons suffering from nervous exhaustion, and though differing in certain respects from the types previously discussed is not always easy to diagnose. Roentgen therapy as employed in seborrhoic dermatitis often gives relief.

The ichthyol-zinc oxide ointment previously described is often satisfactory for use during attacks of dermatitis. In other cases a powder is preferred Lincsz employs the following modification of Unna's powder which is colored to resemble the skin and hence need not be removed daily:

Zinc oxide	5 0 parts
Magnesium carbonate	. 4 0 "
Bolus alba	. 2 0 "
Bolus rubra	. 0 5 "
Rice starch	8 0 "

In this condition and in seborrhœic dermatitis the use of water on the affected skin must usually be avoided during attacks, the skin being cleansed with simple cold cream or aquaphor.

Molluscum Contagiosum.—Molluscum contagiosum affecting the lids is commoner than is usually supposed, and *may give rise to a chronic follicular conjunctivitis.* Any small white nodules near the lid-border should be regarded with suspicion, as this may be the only region affected. The best treatment of this condition is *expression of the nodules with*

trachoma forceps or small thread forceps *after puncturing them with a cataract knife.* The whole content of the nodule can be removed in this way as completely as by excision, and after such expression the conjunctivitis usually clears up rapidly. If doubt exists as to the nature of such a nodule the expressed material should be sectioned, as the histological picture is very characteristic. (See Stellwagon, Diseases of the Skin.)

Pediculosis of the Lashes.—Pediculosis of the lashes is occasionally seen, usually associated with pediculosis elsewhere. The pediculi themselves are very small and remain so closely attached to the lid-border as often to escape observation, when the condition may be taken for blepharitis. The black dots representing the egg capsules can be seen as such with the loupe and a few pediculi can then be found after rubbing the lid-border with an applicator.

Treatment with a *3 per cent ammoniated mercury ointment is usually effective after removal of as many pediculi as possible.*

Intermittent Blepharospasm.—Intermittent blepharospasm, or *tic*, with or without pain, is an annoying and disfiguring occurrence, which is especially common in elderly persons. It may develop into spastic entropion, when the corneal irritation demands surgical intervention. More often, however, the eye is simply shut spasmodically, without entropion, and since the condition develops slowly, without great disturbance of vision, it is left untreated. Safar, Meller and Hughes have shown that the injection of alcohol under the orbicularis at the outer border of the orbit, as is done with novocaine for akinesia, will often give relief for long periods or even indefinitely. One to 2 cc. of 80 per cent alcohol are used, after previous injection of 4 per cent novocaine. This procedure avoids the danger of complete facial paralysis, which has occurred after injections of the facial trunk, and *is accepted by some patients who would refuse an operation* such as resection of the orbicularis at the outer angle. The effect of such injections is in most cases only temporary.

Herpes Zoster.—In herpes zoster affecting the lids the local lesions are practically unaffected by treatment and can only be protected from secondary infection by a zinc oxide ointment or the calamine-zinc-oxide lotion. *The intense pain,* however, *was found by Sidlick to be remarkably relieved for some unexplained reason by the use of intramuscular injections of pituitrin, 0 5 to 1 cc. of the ordinary obstetrical preparation, given once or twice at forty-eight-hour intervals.* The author has seen a number of cases in which such injections were each followed by complete relief of pain lasting two to three days, and not returning after the third injection. No definite effect was seen on the actual lesion in cases of ocular involvement. The use of *convalescent serum* has been discussed on page 128. It has definite advantages, apparently, especially on the course and ultimate outcome of ocular complications, and should be employed when it is available.

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CHAPTER VII.

DISEASES OF THE CONJUNCTIVA.

ACUTE CATARRHAL CONJUNCTIVITIS.

ACUTE *catarrhal conjunctivitis,* or "pink eye," *is in the United States usually due to the pneumococcus,* while in tropical climates and the seacoast towns of Europe the Koch-Weeks bacillus is the most common offender. The pneumococcal form is characterized by intense congestion of the conjunctiva, including the bulbar conjunctiva, and small petechial hemorrhages are often present. It occurs in the presence of acute coryza, but more often, especially in its epidemic form, without any involvement of the nasal mucosa, being possibly due to a special strain of the organism. When seen early ice-packs to the lids will often reduce the swelling, but they should usually be used for only twenty-four to forty-eight hours, after which hot packs seem to be of more value in combating the inflammation. A smear or epithelial scraping should be made to determine the infecting organism, and if it is proved to be the pneumococcus 1 or 2 per cent *optochin hydrochloride* may materially shorten the course of the disease. Optochin is Morgenroth's quinine derivative, ethyl hydrocuprein, which he found to have a specific action on the pneumococcus. Gruter has shown that the conjunctival sac can be rapidly made free of pneumococci and kept so by two daily instillations of 1 or 2 per cent optochin. The solutions should be made fresh as they lose potency rapidly. Such solutions are often quite painful, and in most cases of acute conjunctivitis other antiseptics, such as 1 to 2500 metaphen solution seem to be about as effective. Instillation of an antiseptic should be repeated three or four times a day, *and continued until all symptoms have been absent for several* days. Lancaster and associates have reported favorable

clinical results from the use of mercurochrome in conjunctivitis, usually in 1 per cent solution. Their laboratory work showed, however, that in the presence of serum a 1 per cent solution killed staphylococci only after one hour, and this is in line with later work which indicates that mercurochrome is by no means one of the most powerful antiseptics. Many of the newer synthetic drugs, such as acriflavine and hexyl resorcinol are claimed to be far superior in bactericidal effect and are apparently no more irritating. One of these drugs is metaphen, also a mercury compound. Birkhaug, in comparative laboratory tests, found it to be 857 times as powerful as mercurochrome, and ten times as powerful as hexyl resorcinol, the differences being even more marked in the presence of serum, in which it killed both Staphylococcus aureus and the gonococcus in ten minutes in a dilution of 1 to 16,000. It has been used in ocular conditions by Key, and may be freely instilled in the conjunctival sac in the 1 to 2500 solution. Experimental evidence in favor of acriflavine, zephiran and other antiseptics is discussed on page 87.

When using conjunctival antiseptics *any purulent or mucoid secretion in the conjunctival sac should first be removed by irrigation with normal saline or boric acid solution before these antiseptics are instilled*, as most drugs form chemical combinations with the proteins of such secretions, which weakens their bactericidal power. Thus experimental evidence regarding the effect of chemical agents on bacteria in normal salt solution gives little information as to their effect in the presence of purulent secretion. It is also true that no experimental work can reproduce conditions in the conjunctival sac in which the tears rapidly dilute any chemical agent introduced, so that a 1 per cent solution of silver nitrate, for instance, remains such for only a fraction of a second, and the resulting dilute solution escapes rapidly with the tears. The effect of all these drugs is probably not due entirely to their bactericidal power, but to their stimulating a flow of tears which washes out pus and organ-

isms from the sac, and also to their effect on the epithelium and underlying structures. An application of silver nitrate or any similar caustic causes a loss of the superficial and partly necrotic epithelial cells containing bacteria and produces a local inflammation with increased flow of lymph and leukocytes into the subconjunctival tissues. Such an effect must be graduated so as to avoid damage to the cornea. To obtain this effect one or more office treatments with 1 or 2 per cent silver nitrate or 2 per cent zinc chloride applied to the everted lids and washed off with normal saline or a weaker zinc solution are often useful and may markedly shorten an attack of conjunctivitis. Many cases will show no discharge after one such treatment if it is followed by instillations of metaphen or 0.2 per cent zinc chloride at home for several days. *Such office treatments demand the previous use of a local anesthetic.* In most cases the duration of symptoms with such treatment is reduced to two or three days, and the infectious period is also shortened. Instillations should be continued for several days after all symptoms have abated.

The silver protein preparations have been much used in conjunctivitis, especially argyrol and neosilvol. The only thing that can be said for their use is that they are nonirritating and that they form a coagulum which may carry with it a number of bacteria when it is removed from the sac. Sollman and Pilcher have shown that the amount of active silver in argyrol substance is only 0.4 per cent and in silvol 0.2 per cent as compared to 63.5 per cent in silver nitrate. Thus a 100 per cent solution of argyrol would be equivalent only to 0.6 per cent silver nitrate, while a 300 per cent solution of silvol would be required to equal 1 per cent silver nitrate. It will be seen that the amount of active silver in the usual 10 and 20 per cent solutions of argyrol is very small indeed. Lancaster, however, believed that some bactericidal effect could be demonstrated, 10 per cent solutions of argyrol killing staphylococci in ten to twenty min-

utes in the presence of serum, and pointed out certain advantages over silver nitrate, which is neutralized rapidly by serum or sodium chloride and has a caustic effect that may not be desirable. The amount of active silver in protargol, collargol and albargin is somewhat higher, 7.5, 1.5 and 13.3 per cent respectively, but if the caustic effect of silver is desired there would seem to be little reason for using anything except known dilutions of silver nitrate. While there can be no disadvantage to this in acute conjunctivitis, *the danger of producing localized argyrosis if such treatment is continued must be remembered.* The silver protein preparations also produce argyrosis in certain persons, and the practice of prescribing argyrol drops to be used freely for every conjunctival ailment should be condemned. This is especially true, of course, in chronic conditions such as trachoma.

One should not forget to warn patients and their relatives of the infectious nature of acute conjunctivitis, and to urge proper hygienic precautions. Affected children must be kept out of school until the discharge disappears, and this time may usually be shortened by the office treatments described. With acute pneumococcus conjunctivitis the only object of our treatment is to shorten the period of discomfort and disability, as there are practically no complications Keratitis practically never develops unless some trauma to the cornea occurs, and it is only rarely that a chronic form of conjunctivitis develops from the acute form.

GONORRHEAL CONJUNCTIVITIS.

In the case of gonorrheal conjunctivitis all our efforts must be directed to the *prevention of corneal complications.* The prevention of the disease itself is, of course, even more important. In spite of the remarkable effects of prophylaxis used at birth, since it was first used by Credé, in 1880, it is still not required in some states, and in other states the law provides for its use but provides no penalty for failure to comply with it. *Almost as dangerous as failure to observe pro-*

phylaxis is the tendency to substitute other silver derivatives for the 2 per cent silver nitrate recommended by Credé. Protargol of various strengths, argyrol and neosilvol are used by some obstetricians and, to the author's personal knowledge, in some hospitals of good standing. With the above-mentioned facts as to the efficacy of argyrol in mind, one must consider its use for prophylaxis as nothing more than an irrigation, which is as likely to carry gonococci into the sac as to wash them out. The establishment of such a procedure as a routine measure in hospitals is a complete abdication of the idea of prophylaxis, and ophthalmologists should insist on the use of either a 2 per cent silver nitrate, neutralized by normal saline after fifteen seconds, or 1 per cent silver nitrate not neutralized. It is, of course, important that solutions of silver nitrate shall be kept from evaporation which would involve danger from an increase in concentration of the drug. To avoid this possibility sealed ampules are available containing enough solution for a single use. There is probably justification for the use by some obstetricians of 1 per cent silver acetate. This forms a saturated solution, and hence can never, by error in compounding or by evaporation, be made more concentrated. It is said to be as effective in prophylaxis as 1 per cent silver nitrate. The other precautionary measures, such as preliminary treatment of the vaginal tract in mothers known to have gonorrhea, and the careful cleansing of the baby's face before the drops are instilled should not be neglected.

When conjunctival discharge appears in an infant two to four days after birth, accompanied by even slight inflammatory symptoms, one must decide at once whether a gonococcal infection is present. *If smears of the discharge,* stained carefully by Gram's method, *show no gonococci an epithelial scraping from the inflamed parts of the conjunctiva should always be examined.* The surface should be shaved gently *with a sharp platinum spatula or scalpel,* so as to remove a thin layer of epithelial cells without causing the surface

to bleed. This may reveal countless organisms which, as Lindner has shown, invade and grow in the epithelial cells, and are only found in the secretion after these cells are cast off.

Once the diagnosis is made, the case must be hospitalized, isolated and given the care of a competent day and night nurse. In infants both eyes are usually involved from the beginning, but in a few cases one eye appears normal, and *such eyes should at once be protected with a Buller shield* or a water-tight collodion dressing, which is changed every day to be sure infection is not developing. The infected eye or eyes should be given frequent irrigations, not according to a routine of every two hours or every hour, but *frequently enough so that no secretion is allowed to remain in the conjunctival sac.* In cases with profuse discharge they may have to be repeated every half-hour day and night for one or two days, the intervals being lengthened as the discharge diminishes. As an irrigating fluid, either a saturated solution of boracic acid or normal saline is as useful as anything, the effect being purely mechanical. The lids should be gently manipulated during irrigation so that any secretion clinging to the cornea or conjunctiva is dislodged, and enough fluid should be used to remove all shreds of secretion from the sac. The solution should be directed into the upper and lower folds and not upon the cornea, unless particles of secretion adhere to the cornea. The cornea must never be touched with gauze, cotton, or an attendant's fingers. The lids must be handled gently, with cotton or gauze on the fingers so that they may be opened effectively, and in cases with much secretion vaseline should be kept applied to the lid-borders so that they may not stick together. (Fig. 42.) The surgeon should personally instruct each nurse in the technique of irrigation, which is the most important part of the treatment. At one large hospital, during five years' incumbency of one efficient nurse as supervisor of the ward for ophthalmia neonatorum, not a single cornea was lost except where keratitis was already present on admission.

Next to irrigations, probably the most important therapeutic measure in this disease is *the use of foreign protein injections.* In infants whole milk boiled for four minutes serves admirably for this purpose. While most cases will clear up without corneal complications on irrigations alone, one can never tell which will turn out to be an unusually severe case, and it is probably safest to use milk injections from the beginning in every case. In fact, Pillat has discussed the question of whether or not a physician is guilty

FIG 42.—Method of holding child for examination and treatment of the eye.

of malpractice in cases where foreign protein is not employed. One cubic centimeter is the usual initial dose, increasing to 1.5 to 3 cc., according to the febrile reaction produced. Repetition every third day for three or four doses is probably the best interval when good reactions are obtained, with fever of 100° to 102° F., but where no reaction is obtained for twenty-four hours after the first dose a second larger one can well be given after twenty-four hours. In gonorrheal ophthalmia the most marked effect is on the swelling of the lids, which often subsides rapidly. Pillat has shown that the

gonococci disappear from the secretion and epithelial cells rapidly after effective foreign protein therapy.

The use of the prepared proteins, such as aolan and lactigen, was found by Pillat to be much inferior to that of boiled whole milk which gives a much more constant febrile reaction. Most authors agree that the use of antigonococcic vaccines is in no way superior to that of whole milk and that febrile reaction, which is a usual accompaniment of effective protein shock, is less constantly produced by the vaccine.

The use of *sulfanilamide* and *sulfapyridine* in gonococcal infections has been discussed (see page 101). There is no doubt that either of these drugs in sufficient dosage will, in most cases of gonorrheal conjunctivitis, free the secretion of gonococci more quickly than the use of irrigations and foreign protein alone. Sysi, reporting on 11 cases treated with sulfapyridine, obtained negative smears after twenty-four hours in 6, forty-eight hours in 2, and four days in 2 cases. One other case had a recurrence but cleared up on a second course. Michels in a series of 15 infants given sulfanilamide found that hospitalization averaged 5.8 days after the drug was begun as compared with 28 5 days for 32 cases treated without the drugs. In 15 reports covering 104 cases summarized by Guyton negative smears were usually obtained in two to five days. The usual dosage given to infants was that calculated to produce blood levels of 2 to 5 mg. per cent. Only in the cases of Michels were blood determinations actually made, giving levels of 2 to 5 mg. per cent. This was obtained with a dose of 1 grain per pound per day during four to eight days with equal amounts of sodium bicarbonate. They saw no appreciable signs of cyanosis, acidosis, skin rash, or vomiting on this dosage. Others report similar results with remarkable freedom from corneal complications.

The usual course of gonococcal conjunctivitis in the newborn, when brought under early and competent treatment with irrigations and foreign protein, is not very severe and

corneal complications seldom occur unless the cornea is involved before treatment is begun.

The much shorter duration of the condition, however, under treatment with these drugs, with consequent saving in hospital and other facilities seems to justify their use in nearly all cases. With proper care severe reactions may in nearly all cases be prevented. Irrigations should, of course, be continued until no more discharge is present.

Antiseptics when used should be non-irritating to the cornea, but a drug such as 1 per cent mercurochrome or 1 to 2500 metaphen, instilled three times a day, may hasten the process of resolution by its bactericidal effect. Argyrol is much used, but without serving any useful purpose, in the author's opinion. Silver nitrate was formerly used in the treatment of most cases as well as for prophylaxis. With the use of milk injections and frequent irrigations it is seldom necessary except in a few cases which develop a profuse thin purulent discharge which persists after the swelling of the lids has subsided. Here the astringent effect of a 2 per cent silver nitrate solution may be of distinct value. It should be dropped on the everted lids or painted on with an applicator, pressure on the globe being used to force the retrotarsal fold into view, and the cornea being carefully protected by the lids. It should be neutralized with normal saline after a few seconds. In some of these cases a similar application of 2 per cent zinc chloride washed off with 0.2 per cent zinc chloride seems to affect the secretion more favorably.

The *use of iced applications* is of value in the early stage when much swelling of the lids is present. Such applications should be kept applied at least one-half the time, between the irrigations which are often very difficult to carry out in the presence of so much swelling. Iced applications should probably not be continued longer than twenty-four or forty-eight hours, and with the simultaneous use of milk injections the severe swelling has usually subsided after this period.

Where the cornea is already involved when treatment is

begun, or where it becomes involved during treatment, irrigations should be continued most assiduously, the pupil should be kept dilated with atropine, and more vigorous efforts should be made to clear up the discharge by the use of antiseptics and milk injections. Where a localized ulcer is present direct applications may be made to it, as will be described in Chapter VIII. Usually, however, the epithelium is absent over a large area and the cornea in this area rapidly becomes necrotic. *In such cases usually the only measure which will save the cornea is the immediate covering of the area with a sliding conjunctival flap.* The presence of a purulent discharge is no contraindication to this most valuable emergency measure, as the raw side of the flap is apparently free from bacteria, and its application to the infected cornea furnishes it with lymph and antibodies which help it to overcome the infection, as well as protecting it from contact with the infectious secretions. Usually the conjunctiva is dissected up all around the limbus and far enough back so as to close over the center of the cornea without tension, where it is held with a purse-string suture. The eyes are left open, and irrigations and other treatment are continued so that when the stitch begins to cut out after four or five days the discharge is usually well under control. If the cornea has already perforated, the iris is cut off before the stitch is tied, after first applying trichloracetic acid to the cornea about the perforation so that the flap will remain adherent at this point for some time.

The treatment of *gonococcal conjunctivitis in the adult* differs in certain details from that of ophthalmia neonatorum. The much greater severity of the condition in adults, with a high incidence of corneal involvement, is well known. The use of intravenous typhoid vaccine with effective irrigations greatly reduced corneal complications, but these did occur in a number of cases, even after treatment was begun. The use of sulfanilamide and sulfapyridine has changed the prognosis entirely in this condition. The 50 cases of Sie-Boen-

Liang were all in adults. They received dimethyl disulfanilamide (Uliron) and negative smears were obtained after one day in 44 per cent, two days in 22 per cent and four days in 14 per cent. Only 10 per cent of cases remained positive longer than four days. The 8 cases of L. and R. Fernandez who received sulfanilamide, required longer periods, but very small doses were given. Only one small marginal ulcer occurred in their series. Ten of the cases reported by Bower and Frank were in adults. In their series of 21 cases of all all ages, 18, including all the adults, responded promptly, with negative smears in an average of two days and no corneal involvement occurring after treatment was begun. Other adult cases were included in Guyton's summary and, aside from the short periods of hospitalization, a remarkable freedom from corneal complications was observed.

Hence there is a very definite indication for the use of sulfanilamide or sulfapyridine in every case of gonococcal conjunctivitis of the adult. The same is probably true of cases in children older than one year. Apparently it is not necessary to obtain such high blood levels of sulfanilamide in this condition as in general infections, levels of 6 to 8 mg. per cent having usually proven effective. Dosage sufficient to obtain the desired level promptly should be given, however, and this is best achieved by an initial dose of half the twenty-four-hour dose, followed by 15 to 20 grains every four hours. This is continued until negative smears are obtained and then gradually reduced. Bowers and Frank gave 15 grains of sulfanilamide per 20 pounds of body weight per day divided into 6 daily doses. When negative smears were obtained this was reduced gradually during three days to one-third the original dose and continued at this lower figure for seven to ten days. Relapses have occurred when the dosage was reduced or the drug stopped too quickly. While a definite superiority has not as yet been established for either drug, the greater regularity with which effective blood levels can be obtained with sulfanilamide and the

smaller incidence of gastric intolerance to this drug seem to offer advantages over sulfapyridine and sulfathiazole. Guyton and Woods, however, are convinced of the superiority of sulfapyridine and sulfathiazole over sulfanilamide in gonococcal infections.

Frequent irrigations are as necessary in the adult as in the infantile form of the disease. Their frequency can usually be cut down rapidly, however, after the first few days.

FIG. 43 — Cone of roentgen-ray film used for protection of the cornea in lagophthalmos

Exceedingly important is the use of a Buller shield or a cone of x-ray film (Fig. 43) for protection of the uninvolved eye. The eye may be inspected through the shield, but it should be removed for examination every two to three days, with every precaution against infection at the time of examination.

Whether foreign protein injections should be employed with the sulfonamides must be decided in the individual case. Results with the drugs alone are usually so good that foreign protein will be reserved by many ophthalmologists for the occasional case which resists such treatment or in which the

cornea is already involved when treatment is begun. The same is true of hyperpyrexia by physical means, as described on page 162. A few remarkable results had been reported following a fever of 105° F maintained for six to eight hours by van Poole and others. The inconvenience and expense of the method, however, will usually cause the sulfonamides to be preferred except in cases which prove intolerant or resistant to these drugs.

Corneal complications, when they occur, are treated as described in Chapter VIII, the same indications for the conjunctival flap being present when a large area of cornea is involved. Corneal involvement, when present at the beginning of treatment, has usually cleared rapidly with the use of sulfanilamide and foreign protein injections.

INCLUSION BLENORRHEA.

When conjunctival discharge appears in an infant later *than four days after birth, and no gonococci are found in* smears or epithelial scrapings, inclusion blenorrhea should be suspected and confirmed by the finding of inclusion bodies in epithelial scrapings stained with Giemsa. Isolation and irrigations are begun as soon as the discharge begins, while awaiting the bacteriologic report. When the diagnosis is made the frequency of irrigations may usually be decreased, as it is known that no danger to the cornea exists. The condition, when treated by irrigation and the usual antiseptics, soon passes into a chronic form with almost no discharge but with conjunctival thickening and follicle formation which persists for three to twelve months. This period, during which the possibility of contagion exists, may be greatly shortened by the use of sulfanilamide. Thygeson has shown that inclusion bodies cannot be found after two to four days of treatment and saw the conjunctiva return to normal in two weeks. This experience has been confirmed by Giddens and Howard and others. A dose of $\frac{3}{4}$ grain per pound per day is suitable for infants as well as for the occa-

sional adult patient who acquires the disease, usually by infection in a swimming pool. Use of the drug is more important in these adult cases, as symptoms of swelling and inflammation are often more severe than in infants, and the inconvenieuce of local treatment and sanitary precautions is much greater. The dose is decreased when acute symptoms subside, but a moderate dose should be continued for two to three weeks.

The author has employed copper sulphate solutions in addition to irrigations in this condition, because of its resemblance to trachoma. A 0.4 per cent solution causes burning but is fairly well tolerated when instilled three times a day

OTHER FORMS OF ACUTE CONJUNCTIVITIS.

The other forms of acute conjunctivitis require little additional discussion, as the methods described for acute catarrhal and purulent conjunctivitis apply equally well to them according to the conditions which develop. *Diphtheritic conjunctivitis*, which is exceedingly rare, should be diagnosed early and treated by serum as well as local measures. *When a membrane develops* in gonorrheal conjunctivitis or that due to streptococci *strong astringents such as silver nitrate seem to do more harm than good*, and reliance must be placed on irrigations, hot packs and foreign protein.

TRACHOMA.

Among the types of chronic conjunctivitis by far the most important is trachoma. Although widespread infection among the population is confined to certain localities, every ophthalmologist of experience sees occasional cases in private practice and some cases are under treatment constantly in nearly every large clinic. There seems to be no doubt that the disease is caused by a filterable virus resembling but not identical with that causing inclusion blenorrhea.

Systemic Chemotherapy.—After centuries during which purely local treatment was employed attempts at systemic

chemotherapy have, within the past four years, produced some encouraging results. The reports of Loe and Sie-Boen-Liang on the use of sulfanilamide in trachoma were followed by many others. The cases of Loe were given relatively small doses, $\frac{1}{3}$ grain per pound per day for ten days, followed by $\frac{1}{4}$ grain per pound for fourteen days. On this treatment Loe reported that acute symptoms subsided promptly and in many cases he considered the condition cured. His dosage was employed by a number of other observers, including Gradle, Richards, Forster and Thygeson and others. Their observations confirmed those of Loe and many ophthalmologists came to believe that trachoma could be cured by sulfanilamide alone. Certain observers, however, while confirming the effect of sulfanilamide on the acute inflammatory symptoms of trachoma and especially on pannus and corneal infiltrations, saw less effect on the chronic conjunctival lesions themselves. Sie-Boen-Liang in his original report stated that the drug had no effect on the papillary hypertrophy or follicles, while Spining saw only 1 case out of 15 which he considered cured, and after relief of acute symptoms during the first week of treatment saw no more effect on the conjunctival lesions when the drug was continued for twenty-one to twenty-four days. Julianelle and associates treated 77 patients according to Loe's method. At the end of treatment only 8 cases were asymptomatic, 40 had improved, while 29 were unchanged. After five to six months 22 were re-examined. Only 8 of these showed improvement over their original status, while 14 were unchanged. Inclusions, when present, disappeared rapidly under treatment. In another group with trachoma complicated by secondary bacterial infection the latter cleared up rapidly on sulfanilamide, leaving the trachoma less active, but not arrested. Wilson* concluded from a study of 10 cases that the drug had no effect on trachoma, which was the opinion of Busacca.* Lee and Rottenstein saw good results in over 100 cases, with a

* Quoted by Julianelle *et al.*

dose slightly larger than Loe's. They saw persistence of follicles for long periods, however. Two cases which were refractory to sulfanilamide improved on sulfapyridine. The cases of Cosgrove, in which treatment by mouth was compared with the local use of an 0.8 per cent solution sulfanilamide, showed improvement as a rule which was about equal with the two methods. They were not followed long enough, however, to be considered cured and the dosage given by mouth was very small. Only a few reports on the use of sulfapyridine in trachoma have appeared and these do not indicate any superiority over that of sulfanilamide.

From a study of the evidence, there seems to be no doubt that sulfanilamide is useful in trachoma, especially when corneal ulceration and acute inflammatory symptoms are present. Vision may improve considerably when these conditions clear up The conjunctival lesions, however, while often showing improvement during treatment, remain in some cases unchanged. While an effect on the virus is likely, as Thygeson believes, there is no doubt that many cases resist complete cure by the drug alone. Certainly the conjunctival lesions can be made to improve much more rapidly by the use of the local measures to be described, and it would seem that the ideal method is a combination of such treatment with the use of sulfanilamide

The same may probably be said of the use of antimony as described by Derkac and by Julianelle and associates. Both employed intravenous injections of tartar emetic, the former in 50, the latter in 40 patients. The dosage recommended by Julianelle and his group was $\frac{1}{20}$ grain in 1 per cent solution daily for six days, then $\frac{3}{10}$ grain on the eighth, tenth, twelfth, fifteenth, nineteenth, twenty-second, twenty-fifth, twenty-eighth and thirty-first days. That employed by Derkac was somewhat smaller. In both series, healing of corneal ulcers and clearing of pannus was observed, but the conjunctival follicles were not materially affected. Both groups advised the combination of local measures, grattage or copper sul-

phate, for most effective healing of the conjunctival lesions. The evidence is insufficient for a conclusion as to the superiority of tartar emetic or sulfanilamide, but the inconvenience of the tartar emetic treatment will probably influence most ophthalmologists in favor of sulfanilamide unless later more favorable evidence in favor of tartar emetic appears.

Local Treatment.—After hundreds of years, copper sulphate is still the drug which, by its astringent and probably also its viricidal effect, is probably of most value in the local treatment of trachoma. In early stages of the disease the use of copper alone will cure a number of cases. Applications of the copper sulphate crystal should be made every day in such cases when this is possible, or at least every two days. Such applications should be preceded by 2 per cent cocaine and adrenalin dropped on the everted lids. The local anemia as well as the anesthesia are desirable to further the effect of treatment. A smooth crystal in a holder is then passed lightly over the tarsal conjunctiva of both lids and into both folds, including the angles and the semilunar folds, and after a few seconds the lids, still everted, are washed off with normal saline or boric acid solution. In older cases, with much scar tissue, the application is not so painful and the irrigation may be omitted. Besides these applications, a solution of copper sulphate, 2 grains, and glycerin, 2 drams, to the ounce is used by the patient twice a day. Ointments containing copper, such as the 5 per cent copper citrate ointment, are preferred by many ophthalmologists to the solution, and perhaps allow the copper to remain longer in contact with the conjunctiva. Such treatment continued for a month will cause the disappearance of follicles and the return of the conjunctiva to its normal smooth appearance in a certain number of early cases. *When, after two or three weeks, progress is very slow, and the follicles are still numerous, one should resort to expression of the follicles without further loss of time.* It would still be possible to obtain a cure by the above treatment alone in many cases, but this might require months,

and many cases seem to resist such treatment indefinitely unless the follicles are expressed. When a patient is first seen in a fairly advanced stage, expression should be performed at the outset, followed by the use of copper.

Expression is done with Knapp's roller forceps, Prince's ring forceps, or H. Gifford's trachoma forceps. (See Fig. 3.) The latter is especially useful because of its shape, which enables the smallest portions of conjunctiva to be grasped, the conjunctiva in the angles being reached by the pear-shaped prominence. Such expression should be preceded by injection of the lids with 4 per cent novocaine, children often requiring a general anesthetic. *All the diseased tissue should be grasped firmly with the forceps and milked out between the blades.* The semilunar fold which is usually involved, the caruncle and the conjunctiva at the angles should be included. McHenry has described a useful technique for expressing the caruncle and semilunar fold with ring forceps, the tissues being grasped with toothed iris forceps through one of the rings and pulled up so that they can be grasped by the blades.

This should be followed by an application of the copper crystal, irrigation and the instillation of a few drops of liquid albolene to keep the raw surfaces from adhering. Cold packs are used to minimize the swelling, which is sometimes considerable, and a weak solution of butyn, 0.5 or 1 per cent, is given to use for the pain, as well as narcotics in some cases. The folds should be spread out daily by everting the lids and pressing on the globe, to prevent adhesions. A daily application of blue-stone, though sometimes painful, should be given for a week or two afterward, and the copper solution should be used as before. By this procedure all the active trachoma is not eradicated, but the diseased tissues are crushed and exposed, so that copper treatment is most effective during the first few weeks after expression. One expression followed by copper for several months will often cure even very chronic cases. Others will require a repetition

of the expression, or scarification with a dull scalpel of certain areas still showing follicles or hypertrophy.

A thorough massage with boracic acid powder on a hard cotton applicator is useful in cases where no grossly visible follicles are present, but which show a diffuse velvety thickening of the conjunctiva. This may have to be repeated several times. Roentgen-ray and radium applications have been used recently in some clinics, but the above line of treatment, if patients can be made to continue it long enough, is nearly always effective and avoids the dangers incident to irradiation. The use of subconjunctival injections of copper preparations is exceedingly painful and apparently seldom necessary. Intravenous injections of copper preparations, such as the copper thiosulphate recently recommended by Stastnik, are still on trial, but hardly seem logical in the treatment of such a localized condition. The reports on chaulmoogra oil and the Sculco method of treatment have not been confirmed by most later observers who have tried them, or when compared to series of cases treated with copper, have shown no definite advantage.

Selinger's reports on *the local use of* quinine have encouraged a number of American ophthalmologists to try this method as a substitute for copper. A saturated aqueous solution of quinine bisulphate (1 gm. to 1 cc. of water) is painted on the everted lids and folds after instillation of a local anesthetic. The application to each lid is continued for one minute and the solution is not washed off, though the cornea should be protected by the lids and no excess of solution allowed to run over it. The treatment is followed by a cold application. Applications are given twice a week, the intervals being lengthened as conditions improve. The patient is given a 2 per cent ointment of quinine bisulphate for use in the sac twice a day between treatments. There is no doubt that pain is less severe during treatment with quinine than with copper sulphate, and that the condition of the lids and cornea is definitely benefited by such treatment.

It is especially useful in patients who develop keratitis or acute symptoms of irritation on the use of copper. It cannot be stated that its affects are superior to those of copper, and in most cases, whether copper or quinine is employed, expression of the folds and occasional grattage or massage with boracic acid is equally necessary. The author has seen a few patients who developed keratitis on quinine and improved more rapidly when copper was resumed. Cases of true idiosyncrasy to quinine are not uncommon. Final results in a large series of cases will be awaited with interest.

Treatment with solutions of *copper, zinc and other substances under the influence of an ionizing current* has been advocated by various authors and recently reported upon by Edison. Special applicators which cover the eye are employed with a high-frequency current of low milliamperage (1 to 2 milliamperes). The method is painful, and perhaps its effects are no different from the use of similar solutions after grattage, but it may be tried in very obstinate cases.

Excision of the tarsus should be reserved for a few chronic cases in which all other methods have failed, or for patients whom one is sure will not return for after-treatment. By this operation it is seldom that all the trachomatous tissue can be removed, and any ophthalmologist living in a trachomatous region has seen many patients on whom it has been performed who later developed all the corneal complications of trachoma with in addition, trichiasis, which is especially difficult to deal with after tarsal excision. In very profuse trachoma one is sometimes justified in excising the upper fold with a strip of tarsus not over $\frac{1}{4}$ inch wide, following expression of all other follicles. Complete excision or turning of the tarsus by Blascovics' method may also be necessary where the tarsus is so incurved as to irritate the cornea, but as much healthy conjunctiva as possible should always be preserved and the region of the secretory ducts of the lacrimal gland must be treated with respect, or the dreaded condition of xerosis conjunctivæ is apt to result.

When *corneal complications* occur the usual treatment of keratitis is indicated. Many small infiltrates will heal promptly on the use of atropine and proper treatment of the conjunctiva. In the presence of keratitis, copper sometimes seems to aggravate the condition and may well be replaced by 2 per cent silver nitrate or quinine bisulphate. In some cases a prompt expression of the folds relieves the keratitis, but frequent irrigations should be employed after the expression and a bandage should never under any circumstances be employed as this causes the retention of irritating secretion. *When trichiasis is present this should, of course, be corrected*, the lashes, if few in number, being destroyed by electrolysis or electrocoagulation or, if numerous, by operation. The van Millingen operation which employs a free graft of mucous membrane from the lip, as modified by H. Gifford, usually gives excellent results in such cases.

For trachomatous pannus a number of measures have been employed, with more or less success. Probably the most important measure is the destruction of all active trachoma of the conjunctiva, after which the cornea will clear up considerably with remarkable improvement of vision in many cases. Drugs such as jequirity and dionin have been much used to produce further clearing of the cornea and may be of some value. Peritomy and more recently, the use of a mucous membrane graft on the denuded sclera around the limbus after the manner of Denig have also many warm advocates.*

The local treatment described may be modified in many cases when it is combined with one or more courses of sulfanilamide. After expression of the follicles, patients on sulfanilamide may show such improvement in the conjunctival

* It has always been the author's impression that the new vessels serve a necessary function of nourishment or removal of pathological products in the diseased cornea, and that any disturbance of such vessels would be followed by areas of necrosis or opacity, so he has hesitated to employ such measures. Denig's reports, however, and the results observed in a number of cases operated upon by Suker at Cook County Hospital, have made him more inclined to try the Denig procedure.

lesions that applications of copper may be reduced to a minimum. In some cases cleansing solutions and instillations of 0.4 per cent copper sulphate will produce healing. When corneal lesions occur, a course of sulfanilamide is indicated and astringents may be discontinued until healing has occurred.

MORAX-AXENFELD CONJUNCTIVITIS.

The *form of chronic conjunctivitis* which is next in importance to trachoma is that caused by the Morax-Axenfeld bacillus. While the corneal complications of this disease are rare and seldom cause extreme visual disability, it is widespread, especially among the peasants of Europe, the Russian-Jewish population of our cities and the farmers of the Middle West, and since it has no tendency to spontaneous cure, the amount of discomfort and partial disability caused by it is not inconsiderable. The Morax-Axenfeld bacillus, which has been found only on the conjunctiva, cornea and nasal mucosa, lives by preference on transitional epithelium, and hence affects especially the inner and outer angles of the conjunctival sac, where the resulting inflammation and secretion produced are especially notable. It produces marginal ulcers of the cornea in a small number of cases, as do its relatives, the bacillus of Petit and Bacillus duplex nonliquefaciens, and more rarely a typical serpent ulcer may be caused by this group of organisms. As is well known, *the zinc salts have an almost specific effect on these organisms,* and the value of an exact diagnosis of conjunctivitis due to this group by careful examination of smears lies in the indication for zinc treatment so afforded. Some patients showing very few signs of angular conjunctivitis, and complaining only of slight irritation which might be ascribed to eye-strain, are refracted many times without relief and clear up promptly only when a smear gives the diagnosis and zinc is used. *Bacteriological examination in every case of chronic conjunctivitis will increase the number of cases in which a diag-*

nosis of this condition is made, and effective treatment employed. Zinc sulphate was the drug originally employed, and a solution of 2 grains to the ounce, instilled two or three times a day, may give complete relief in mild cases. Zinc chloride is about twice as active and also twice as irritating, so that a concentration of 1 grain later increased to 2 grains to the ounce, is usually as strong as can be advised for home use. In chronic cases of any severity, however, in addition to such treatment, *applications by the ophthalmologist of a stronger solution are usually necessary,* and in any case such applications will hasten the process markedly. Two per cent cocaine or butyn should first be dropped on the everted lids, and after a minute 2 per cent zinc chloride is dropped on, worked into the folds and washed off after thirty seconds with 0.2 per cent zinc chloride. This should be repeated two or three times a week for several weeks, the weaker zinc being used at home during this time, and continued for a month after all symptoms have subsided, as the disease is very prone to recurrence. When the skin at the outer angle is chapped or fissured, as is often the case, it should be protected by zinc oxide ointment. Treatment of the corneal complications will be discussed in Chapter VIII.

STAPHYLOCOCCIC CONJUNCTIVITIS.

The studies of Thygeson, O'Brien and Allen have shown that a form of conjunctivitis with fairly definite characteristics is caused by *strains of the staphylococcus which form a soluble toxin.* While staphylococci are so common on the last border and conjunctiva that their presence may be considered normal, Thygeson showed that strains which ferment mannite are nearly always toxin forming and hence the presence of a number of colonies of such organisms must be considered probable evidence that they are the cause of the conjunctivitis. The diagnosis requires cultures of secretion or epithelial scrapings on Difco plates containing 1 per cent mannite, organisms which ferment this sugar turning the

plate yellow. The author prefers making a primary culture on a blood plate, by which not only staphylococci but other organisms may be detected, and transferring colonies of the staphylococcus to a Difco plate. Any bacteriological laboratory may be instructed as to the information required.

The form of conjunctivitis described by Thygeson is of an exceedingly chronic type, often associated with blepharitis or with a history of blepharitis, with a tendency to frequent exacerbations during which small marginal infiltrations of the cornea may occur. It responds poorly or not at all to the usual antiseptics, but yields, in many cases, to a course of *Staphylococcic Toxoid.* Thygeson employed Lederle's Toxoid, Dilution No. 2, in dosage increasing from 0.05 to 1 cc. Injections are given twice a week until 1 cc. is given, which is repeated weekly for several weeks. The author has felt that *improvement was more consistent when the toxoid was also employed locally.* Full strength toxoid produces definite local reactions but by first using 0.3 cc. of Toxoid No. 2 to 10 cc. of normal saline and increasing this in steps of 0.6 to 9.4, 1 to 9, 2 to 8, 3 to 7, 4 to 6, 5 to 5, 4 to 6, 3 to 7, and 2 to 8 cc., reactions are usually slight or absent. When reactions do occur, the previous dilution is continued for a longer period. Usually each solution is used for two weeks, when the next stronger dilution is employed. In certain cases the dilutions cannot be increased beyond 4 to 6 without reactions. The strongest solution employed is continued for periods of several months, which seems to prevent recurrences. No other ophthalmologists have reported on the use of this method, but the author has been encouraged to continue it in cases showing strains of staphylococcus which ferment mannite.

In cases showing blepharitis or meibomitis, these conditions are treated as has been described. No other local treatment to the conjunctiva is employed except the use of an alkaline wash (Alkaline Buffer No. 1). Thygeson* after trying vari-

* Personal communication.

ous local antiseptics, has concluded that a 5 per cent ointment of sulfathiazole sodium is the most valuable agent in this condition. It is used on the lid-borders and in the conjunctival sac. The ointment is made in a 50 per cent lanolin and 50 per cent petrolatum base.*

OTHER FORMS OF CHRONIC CONJUNCTIVITIS.

A miscellaneous assortment of conditions showing conjunctival congestion, secretion and lacrimation is often lumped under the term chronic conjunctivitis. In order that any effective treatment may be employed, this ophthalmological scrap-heap must be broken down, so far as possible, into groups of similar etiology.

The group due to *bacterial infection*, in addition to the types of chronic conjunctivitis just described, will include cases due to the pneumococcus, which may cause chronic, as well as acute conjunctivitis, the streptococcus and other less common bacteria. Bacteriologic examination is necessary for diagnosis in this group and for exclusion of cases which must be placed in other groups. It should be made before any treatment is employed. Cases due to the pneumococcus respond well to 1 per cent optochin hydrochloride. In other forms of proven bacterial conjunctivitis various antiseptics may be employed, including local applications of silver nitrate, copper or zinc to the lids. When a determined effort is made to obtain a definite diagnosis in this group, the cases requiring such local treatment will be found to decrease markedly in number. In obstinate cases due to the pneumococcus or streptococcus, a course of sulfapyridine or sulfanilamide may aid in arresting the condition permanently.

In the group due to *irritation by chemical agents* the use of antiseptics serves only to further aggravate the condition. A number of cases are seen, in fact, in which such treatment is the only cause of continued irritation, the original infection, if one was present, having long ago subsided. Diagnosis

* While symptoms are usually relieved by such local treatment, Thygeson has found that recurrences are much less common when active immunization with the toxoid is carried out at the same time.

requires a careful history and exclusion of bacterial infections. Such care as is possible to eliminate these irritants by avoiding smoking cars and poorly ventilated rooms, the use of close-fitting goggles when swimming in pools or working in the fumes of chemicals will usually give marked relief. Immediate relief is afforded by a mild alkaline solution with, in some cases, use of a weak and harmless local anesthetic such as 0.5 to 1 per cent novocaine hydrochloride with 1 to 4000 epinephrine.

It is necessary to separate from this group *cases due to allergy*, or sensitization to some specific agent or group of agents. Here again the use of an alkaloid, such as eserine or pilocarpine, may be responsible and relief is obtained promptly on removing or changing the drug There is a tendency to classify as allergic many cases for which no definite cause can be found. It is nearly always possible, however, to obtain a history of exacerbation after certain contacts in true cases of allergy, and such cases should present certain fairly definite signs, such as itching, chemosis, follicle formation or transient chemosis. Such cases are to be distinguished from vernal conjunctivitis, which will be discussed later, but do include the common conjunctivitis which occurs with hay fever. The finding of eosinophils in smears of secretion stained by Giemsa or Wright's stain, with absence of pathogenic bacteria, is very suggestive of conjunctival allergy. In such cases elimination of various agents, as described on page 208, including cosmetics, perfumes, hair and lash dyes, and eye drops of unknown composition, will often give prompt relief. Relief on change of climate or domicile suggests house dust or common molds as the agent. Skin tests for these and other agents are sometimes necessary. When findings are positive, desensitization may be necessary and may give valuable results. This is especially true, of course, in the conjunctivitis accompanying hay fever. The symptom of itching is relieved to some extent by the use of epinephrine in 1 to 4000 or 1 to 3000 dilution. Astringents and antiseptics are usually contraindicated.

In certain *cases of eye-strain* signs of moderate conjunctival irritation are present. These are relieved by proper refractive correction, and a refraction should not be omitted in cases not falling into any of the above groups.

Various *systemic affections*, including the anemias, show similar symptoms and general examination is not infrequently called for in obstinate cases without infection or other local causes. The group of cases associated with *deficient lacrimal secretion*, known as *kerato-conjunctivitis sicca*, is discussed on page 264.

Folliculosis in children should require no local treatment, as it is merely a form of lymphoid hypertrophy without deleterious results. Under care of the general health, removal of diseased tonsils and aderoids, adequate diet and plenty of fresh air it disappears spontaneously. Follicle-formation may be so profuse as to cause confusion with trachoma or inclusion blenorrhœa, and in such cases, or in cases with any secretion, a 0.2 per cent zinc chloride solution may be employed while the child is observed until a diagnosis can be made.

VERNAL CONJUNCTIVITIS.

Vernal conjunctivitis, or vernal catarrh, is an interesting condition about whose cause we still know very little. It has been somewhat vaguely connected with the vagotonic constitution and endocrine imbalance by Angelucci and his followers, and we do know that it occurs commonly in children or adolescents with adenoids, enlarged cervical glands and the disorders attending puberty, and that some cases show an eosinophilia of the blood, as well as the marked increase of eosinophiles in the secretion which characterizes the disease. It has also a definite relation to summer weather, though whether the light or heat is most at fault is not known. Some cases are undoubtedly, as Lemoine and others have shown, sensitive to certain proteins, chiefly pollens, which are present in summer, but this does not apparently

explain all cases. While the condition is most common in warm climates, it is common enough in most parts of the United States so that every ophthalmologist should see several cases every year, if he is on the lookout for the milder forms of the disease, with only moderate pericorneal congestion, but with a definite seasonal incidence and the complaint of itching.

In milder cases the use of epinephrine will give so much relief that more radical measures are not required. A 1 to 4000 solution, with 40 grains of boric acid to the ounce added as a preservative, is instilled four to six times a day, or often enough to relieve the itching, and iced compresses are used with this. Dark glasses give relief on sunny days. In more severe cases, with hypertrophy around the limbus or large papillæ of the palpebral conjunctiva, or in apparently mild cases where symptoms are not relieved by epinephrine, a more systematic examination should be carried out which may afford indications for treatment. *Skin tests with the common proteins may reveal sensitization to pollen or a food* which may be avoided or to which the patient may be desensitized. Some observers, such as Wood, have reported a deficiency of blood calcium in some cases, which seems to justify the use of calcium. In these cases subcutaneous injections of epinephrine, 3 to 5 mm. of 1 to 100, repeated once or twice a week, as warmly advocated by Baldassare and other Italian observers, may be tried.

All these forms of treatment, except desensitization, are purely symptomatic, giving relief only during the season when they are used, with recurrence of symptoms the following season. The *use of radium*, however, has in many cases given permanent relief, with replacement of the papillæ by smooth scar tissue. *It should be reserved for cases with troublesome symptoms which have resisted other forms of treatment.* Quick has warned against the dangers of radium, having seen cataract develop in several cases following its use. Where the limbus is not involved the cornea may be pro-

tected to some extent by a shell like that used for roentgen-ray treatment, but this is far from affording absolute protection against radium as it does against roentgen-rays.

For the technique use by Dr. Laura Lane, which has given some excellent results in the author's hands, see Chapter V. A *calcium chloride and urea compound* known as Afenil, injected intravenously, was first employed by German ophthalmologists in this condition, and some cases experienced great relief from the symptom of itching when so treated. In other cases the method was without effect. A disadvantage of afenil is the necessity for great care in injecting it, as the injection of a few drops outside the vein causes necrosis. This is avoided by the use of *calcium gluconate*, which may be injected subcutaneously or intravenously, 10 cc. of a 10 per cent solution daily being the usual dose. Calcium gluconate by mouth is probably as effective, but larger amounts must be given, usually 75 grains t. i. d. The less expensive *calcium lactate* in doses of 15 to 30 grains t. i. d. is probably as useful. If viosterol is given at the same time, less calcium is necessary.

In many cases one cause of discomfort is the presence of dry, ropy secretion on the conjunctiva. Lehrfeld has found that the use of an alkaline solution which dissolves this secretion is of value. He recommends a 3 per cent sodium carbonate solution, but as stated in Chapter III, this is so alkaline as to cause symptoms of irritation in some patients, and the author has found a 3 per cent solution of sodium bicarbonate or the Alkaline Buffer Solution No. 2, which has a reaction of 8.4, more useful. If epinephrine is being employed, it should not be given within an hour or more following the alkaline solution, which precipitates it.

CONJUNCTIVAL ARGYROSIS.

This disfiguring condition is the result of long-continued use of silver preparations, including the silver proteins, or of misdirected attempts to inject such solutions into the

lacrimal sac. Where it involves the bulbar conjunctiva in its visible portions, it may well be treated by the method of Stillians and Lawless which was first applied to conjunctival argyrosis by Weymann. It consists in the injection of reducing substances under the conjunctiva. The solution employed is a mixture of 12 per cent sodium thiosulphate and 2 per cent potassium ferricyanide. The solutions are made in sterile distilled water and mixed in equal parts just before injection. A platinum needle must be used to avoid the staining produced by action of the solutions on a steel needle. Five per cent cocaine may be injected subconjunctivally first, followed by 0.6 to 0.9 cc. of the mixed solution. The affect on the stain is almost immediate blanching. The reaction is only moderate and when it subsides additional areas may be similarly treated. When the skin over the lacrimal sac is stained this may be treated in the same way except that injection must be made *intradermally* which is a delicate procedure in this region where the skin is exceedingly thin.

PEMPHIGUS CONJUNCTIVÆ.

This rare condition, whether occurring with skin lesions or as the only manifestation of the disease, is a serious one. The folds are obliterated by repeated shallow ulcers which heal with great scarring. Gradually the bulbar conjunctiva becomes involved and the corneas are lost by recurrent ulceration or necrosis. Trichiasis occurs frequently and hastens the corneal complications.

Treatment has usually been confined to correcting trichiasis when it occurred by grafts of mucous membrane into the lid-borders. Recently Dupuy Dutemps has reported the successful use of large mucous membrane grafts to replace the atrophic bulbar conjunctiva, with preservation of the cornea for long periods. Lawless has also had encouraging results with the combined use of *Germanin* and a mixture of vitamin concentrates. Germanin is a proprietary preparation,

a complex urea derivative, the exact formula of which is not published. It is injected subcutaneously, $\frac{1}{2}$ to 1 cc. being given in 3 injections, three days apart. This is repeated after a month if necessary. The vitamins, which are given at the same time and continued for long periods, are conveniently used in the following mixture:

Carotene (vitamin A)	10 cc.
Viosterol (vitamin D)	20 cc.
Wheat germ oil (vitamin E)	30 cc.

Sig. 20 gtt. b.i.d.

This method of treatment has apparently affected the condition favorably and a few cases have become stationary while it was employed.

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produce a thin syrup which is easy to apply. A convenient way to apply it is on a wisp of cotton wound on a pointed

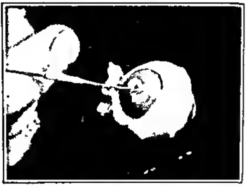

Fig 45.—Application to surface of corneal ulcer with flexible cotton point.

Fig. 46—Application to deeper ulcer with hard point.

applicator and cut off to form a fine point. This should be tried on a finger-nail to be sure an excess of acid is not present. If the infiltrate is deep or covered by soft exudate

a hard applicator must be made, by winding a very small wisp of cotton tightly around a sharp-pointed applicator. (Figs. 44, 45 and 46.)

If the infiltrate has been developing for several days when the patient is first seen there will usually be considerable pain and congestion. In this case atropine and hot packs should be used from the beginning as for any corneal ulcer If the condition does not seem severe enough to justify the use of atropine, homatropine may always be used to produce a temporary relief from ciliary spasm.

SERPENT ULCER.

When we should apply the name serpent ulcer to such a condition is unimportant. *Any corneal infiltrate which causes persistent pain and congestion and tends to spread deeply in the cornea contains pathogenic organisms,* usually pneumococci or streptococci, *and is a severe corneal infection, capable of compromising the entire globe.* Such cases should be hospitalized when possible, chiefly so that we may not fail to see them every day. Where one or two applications such as above described have been made, and the infiltrate continues to spread, we must not hesitate to use more heroic measures. Non-specific protein therapy will be of value here in many cases, and should be used early.

The local antiseptic treatment may also be varied, first by making it more thorough, getting well into the bottom and edges of the ulcer with a sharp hard applicator, and second by changing the antiseptic. Tincture of iodine is very hard to apply, but when made into a *thick saturated syrup of iodine* it is easy to apply and sometimes very effective. This is done by adding 5 drops of the tincture of iodine, 5 drops of glycerin, and 1 drop of a saturated solution of potassium iodide to 10 grains of iodine crystals. A similar iodine preparation was used by Verhoeff. Such a syrup may be applied very thoroughly to an ulcer, twice a day if necessary, without danger, although severe pain is often complained of following the treatments. Such applications

should be made at least once a day and accompanied by plenty of atropine and heat. Another antiseptic which is sometimes useful is mercurochrome, used as a thick paste made by adding a drop of water to a few crystals of the drug. This, when applied as described above, stains the ulcer a deep red, the red color persisting twenty-four hours or longer.

Early bacteriological study of such corneal infiltrates is often exceedingly useful and should never be omitted. A small amount of exudate removed with the spud from the area of active infiltration will usually show the responsible organism. If it is the pneumococcus, application to the ulcer of a few granules of *optochin hydrochloride* will often sterilize it. If this organism, the streptococcus or the staphylococcus are found indications for systemic chemotherapy, which will be discussed later, are afforded. If members of the Morax-Axenfeld group of bacilli are present, use of *30 per cent zinc chloride* by careful local application seems to be superior to other antiseptics. These organisms, as is sometimes forgotten, occasionally cause severe serpent ulcers and it is a mistake to assume that all serpent ulcers are caused by the pneumococcus.

In a large number of cases these measures will prove successful, especially if the infiltrate is seen early, and if so the congestion will decrease, the pupil will dilate easily and the pain will disappear. Any increase of pain or congestion, or the resistance of the pupil to atropine usually means further progress of the infection. In such cases, besides repeating our foreign protein in increased dosage, the local infection must be treated more radically. This is where the actual cautery was, and in some hands, is still used to burn away completely the site of infection. This leaves very dense scars, and can be avoided in most cases by prompt *opening of the anterior chamber.*

The cornea is subjected constantly to the intraocular tension and under normal conditions this does not interfere with its nutrition. When infection is present in this avascular

tissue, however, it is of advantage to relieve it from this normal tension, allowing an increased supply of lymph and antibodies to penetrate it from the limbus. When the ulcer is seen at a very early stage, it may suffice to perform paracentesis at the limbus, emptying the anterior chamber completely. In any well-advanced ulcer with hypopyon, however, it is necessary to repeat the decompression of the cornea daily or even oftener. This may be done conveniently by the method of Harold Gifford, which he called delimiting keratotomy. It consists in an incision through the cornea, not at the limbus, but tangential to the advancing border of the ulcer. The pupil is first dilated widely with atropine or neosynephrine to prevent iris prolapse. A retrobulbar or subconjunctival injection of 4 per cent novocaine is necessary and a preliminary narcotic is advisable. The ulcer is then treated thoroughly with any desired antiseptic. With good fixation of the globe at a point opposite to the proposed direction of the cut, the cut is made with a small, very sharp Graefe or Wheeler knife. The knife is held with the edge towards the operator, is inserted obliquely opposite one side of the ulcer, and passed across the chamber until it can be seen beneath the opposite border, when the cut is completed. (See Fig. 47.) Although the knife enters the cornea obliquely, so that the lens may not be wounded, it is important that it shall enter the chamber. Some aqueous usually escapes with the knife, when the remainder is allowed to escape more slowly by depressing one lip of the wound. Hypopyon, when present, escapes with the aqueous, but any which remains is usually absorbed within one to three days. Reopening of the chamber is easily performed after a few instillations of a butyn or pontocaine by depressing one lip of the wound with a thin sharp instrument such as a spatula or cystotome. It may be necessary to insert this into the chamber to allow the escape of aqueous. Reopening should be repeated daily until the ulcer no longer stains which in the case of a large ulcer may require five to ten days. When the ulcer is exactly cen-

tral and advancing in all directions, it may be best to make the incision across its central portion as in the original Guthrie-Saemisch method, or to perforate it with a fine cautery-point. Marked improvement in all signs of infection nearly always occurs within one or two days following the procedure, and healing is rapid. (See Fig. 48.) Whether or not, as H. Gifford supposed, the growth of epithelium into the wound acts as a barrier to infection, ulceration rarely progresses across the incision if this is made in clear cornea just in advance of the ulcer. If the cut is not long enough,

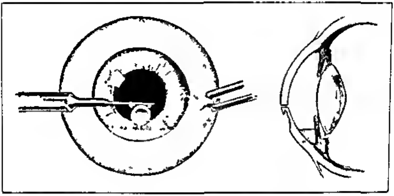

FIG. 47.—Technique of delimiting keratotomy.

progress may occur around one end, when a second cut is occasionally necessary. The scar of such an incision is inconsiderable when compared with that of the ulcer itself. The fear of carrying infection into the anterior chamber has proven groundless, the escaping aqueous acting as a preventive. The lens should never be wounded if the procedure is performed under proper conditions, with good fixation. The author is convinced of the great value of this procedure, and advises that it be employed early, before the most valuable part of the cornea has been destroyed.

The treatment described above, especially early keratotomy combined with foreign protein therapy, is usually suc-

cessful in stopping progress of the ulcer with preservation of the cornea which is still clear at the time of keratotomy. A few very virulent infections, however, are not controlled by these means and hence *the results obtained by the* sulfonamides *in serpent ulcer are of considerable importance.* These drugs are of especial value in the hands of ophthalmologists who do not employ early keratotomy. Roggenkamper employed sulfanilamide in 15 cases of serpent ulcer, both by mouth and by subconjunctival injections. Although neither

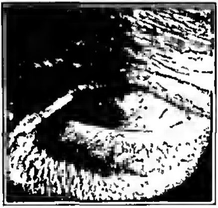

FIG. 48.—Serpiginous keratitis showing effect of delimiting keratotomy

exact dosage nor bacteriological findings are given, he reports that all cases healed promptly so that it was unnecessary to perform Saemisch section. Rosengren treated 5 cases of serpent ulcer and 1 of infected corneal wound with sulfapyridine. Although pneumococci were found in only 2 cases, it was considered that all were probably pneumococcal. All healed promptly and apparently without local treatment except atropine. Szinegh employed sulfapyridine in 10 cases. The improvement in visual results in this series, as compared with those in the two previous years treated by the usual methods but without the drug, was striking. In 1937 and 1938, 27.64 per cent of eyes lost all vision while

only 9 and 7 per cent respectively had enough vision left for rough work. In the 1939 series no eyes lost all vision, while in 40 per cent vision was good enough for rough work, in 20 per cent it was enough for reading and in 10 per cent it was almost normal. Guyton treated 1 severe serpent ulcer due to the streptococcus with sulfanilamide by mouth and locally with 0.8 per cent solution and saw remarkably rapid healing. In a series of cases seen at Cook County Hospital during 1939 and 1940 sulfanilamide was given by mouth. In spite of the fact that a number were probably due to the pneumococcus, there seemed to be no doubt that healing was more rapid and that keratotomy was less often required than had been the case before such treatment was begun.

The use of systemic chemotherapy should be combined with local treatment. It is certainly of advantage to identify the organism responsible for every serpent ulcer before deciding which drug is to be employed. Pneumococcic ulcers do better on sulfapyridine or sulfathiazole while in those due to the streptococcus, often especially severe in character, sulfanilamide is the drug of choice. In diplobacillary ulcers sulfanilamide may well be employed since Julianelle saw conjunctival infections due to this organism clear up rapidly on the drug. The report of Guyton on the use of a 5 per cent sulfanilamide ointment locally (page 104) indicates the possible value of this method. The ointment was used every hour day and night and the importance of frequent applications was emphasized.

MARGINAL OR CATARRHAL ULCER.

These names are used to describe a group of superficial ulcers due to various agents. They occur, as a rule, near the limbus and run a benign course, tending to heal spontaneously. They occur not uncommonly in the course of diplobacillary or Koch-Weeks conjunctivitis, but also without any apparent conjunctival infection. Treatment of the conjunctivitis, when present, will usually bring about healing and

prevent recurrences. Healing is greatly hastened in any case, however, by *one or two careful applications of pure trichloracetic to the ulcer.* Small ulcers often heal within twenty-four hours after such an application, while larger ones require several daily treatments. There is some evidence that deficiency in vitamin A may play a part in the recurrent catarrhal ulcers of elderly persons, and they seem to be prevented by an adequate supply of this vitamin.

MOOREN'S ULCER.

This condition is known also as rodent ulcer of the cornea or chronic serpiginous ulcer, but has nothing to do with either rodent ulcer of the skin (carcinoma), or ordinary serpiginous keratitis. It is a rare form of infection, or dystrophy, which begins at the limbus, resembling in its earliest stages a catarrhal ulcer. It progresses steadily, however, both centrally and around the limbus, healing from the limbus as it goes, but in most cases never healing completely until the whole cornea is covered by a scar dense enough to prevent useful vision.

Fig 49.—Mooren's ulcer progressing after sliding conjunctival flap. Effect of delimiting keratotomy down and out.

Every variety of treatment has been tried but the usual antiseptics and use of the actual cautery have in nearly all cases been ineffective. Since the subconjunctival tissues seem especially involved in this condition, attempts have been made to destroy this whole area with the cautery, and in a few cases this has been successful. The author has seen it fail entirely in other cases.

The only measures which have met with fairly consistent success in this condition are *the use of a sliding conjunctival flap*, which is made large enough to cover the ulcer and a certain amount of healthy tissue central to it, *and the employment of delimiting keratotomy.* When the flap is employed it is well to treat the ulcer and under surface of the flap with trichloracetic acid so that a firm adhesion will form. The flap should not be removed from the cornea until all danger of recurrence is over, a matter of many months, and it is sometimes safest to leave it in place indefinitely. *Keratotomy has been more uniformly successful in the author's experience.* It is simpler to perform and avoids the deformity of the flap. It is made just in advance of the most active area of ulceration, and the incision is re-opened daily for twelve to fourteen days or for a longer period if active ulceration persists.

SMALLPOX KERATITIS.

Another exceedingly serious form of corneal infection is the smallpox infiltrate. This condition is not so common now as in the prevaccination days when it formed one of the most important causes of blindness. The lesion usually comes on during the stage of eruption, but instead of clearing up with the skin lesions, it goes on with a sluggish progress through the cornea. *The only form of treatment which seems to effect these lesions favorably is keratotomy, the chamber being kept open for one to two weeks.* It often fails entirely, however, and probably the most important thing to do on first seeing such a case is to give the prognosis for a long illness, with very doubtful outcome.

PHLYCTENULAR KERATITIS.

Depending upon entirely different causes from the types of ulcer just considered, phlyctenular keratitis requires a different line of treatment. Here *the cause is a constitutional one,* and probably in the great majority of cases tuber-

culosis of the glandular type is at fault. Apparently the most plausible explanation of this puzzling condition is a sensitization of the organism to tuberculous or other toxins, so that when small emboli of organisms, probably dead or attenuated, lodge in the capillary loops at the limbus a local reaction occurs which produces the phlyctenule. The cases in which these lesions continue to recur in adult life are rare, but may cause serious visual disability where the central portion of the cornea is involved. *The important thing is constitutional treatment, by diet, cod-liver oil or concentrates containing vitamins A and D, and sunlight. Calcium is probably also of definite value* in this condition, and Cremer has warmly recommended it in the form of calcium gluconate. This contains 9.3 per cent calcium, is tasteless and well tolerated; 1.5 drams of the powder, three times daily, are given to children over three years of age and 1 dram, three times daily, to those below this age, the treatment being continued for several weeks. Control of diet and hygiene are impossible in the home in many of these cases, so that a period of hospitalization is often necessary. During this period contributing factors, such as infected tonsils, adenoids and sinuses, which are frequently present, should be dealt with. These probably secondary factors are so commonly present that some pediatricians consider them the cause of phlyctenulosis. At the end of hospitalization, a vigorous attempt to instruct the child's family in hygiene should be made, and where the child is not doing well at home, control of home conditions by visiting nurses should be repeated. A recent addition to the general treatment of this condition which seems to be of definite value is *the use of artificial light-baths* with the Finsen light or some form of mercury vapor arc light. (See page 150.)

Locally, *atropine is apparently of definite value*, perhaps by relaxing the ciliary spasm present and consequently the severe blepharospasm, which causes retention of secretion in the conjunctival sac. Yellow oxide of mercury ointment

in the sac is usually used, and apparently cuts down the number of organisms in the sac which may secondarily invade the ulcerated areas. Local applications of trichloracetic acid, or phenol, though difficult to make in young children, seem to be of very definite value, both before and after the lesion has broken down. They need not be repeated so often as in serpent ulcer, and often one or two applications at two- or three-day intervals will be sufficient.

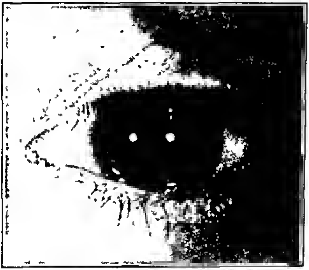

FIG 50 —Deep, rapidly progressing central phlyctenule showing effect of delimiting keratotomy.

Where the infiltrate is central and tends to extend deeply into the cornea prompt opening of the anterior chamber is indicated, in the author's opinion. With such a lesion delimiting keratotomy is not necessary, but only a puncture through the ulcer with a small cataract knife. This may require brief general anesthesia, but is often possible with thorough local anesthesia.

Local phototherapy has not been generally successful in this type of keratitis. Tuberculin is also disappointing

here, and the severe focal reaction often produced is considered by most clinicians as contraindicating its use in phlyctenulosis.

SCLEROSING KERATITIS.

Another form of keratitis which is considered as *usually due to tuberculosis* is sclerokeratitis or sclerosing keratitis. This begins in the sclera and episcleral tissue near the limbus and soon involves the cornea, causing extensive opacity and even ectasia. Here general treatment must be considered, as in phlyctenulosis, though the condition usually involves adults, often in apparently good health and living in average conditions of hygiene. As in most other tuberculous conditions of the eye, the patients are not subjects of demonstrable pulmonary tuberculosis, and general examination will usually show only the roentgen-ray picture of enlarged peribronchial lymph glands. The tuberculin test is usually positive, and by this is meant not the von Pirquet, which in an adult would be of little significance, but the subcutaneous test with Koch's old tuberculin, or the intradermal test with high dilutions of old tuberculin. *Where one of these tests is positive, a course of tuberculin is indicated* regardless of the absence of other general findings indicative of tuberculosis. In spite of the discouraging reports of Derby and Carvill on tuberculin treatment in ocular conditions, and in spite of some theoretical objections to its rationale, the clinicians most familiar with tuberculosis of the eye still consider it an important part of their therapy. The author has watched a number of cases of sclerosing keratitis treated with and without tuberculin, and the favorable course of those given tuberculin seemed to offer fairly definite evidence of its value. (See Chapter IV.)

Local treatment has usually been limited to atropine during the periods of congestion. Local phototherapy, however, has apparently given some good results here in the hands of Stock, Gilbert and others, and is well worth a trial. The

Birch-Hirschfeld lamp with uviol filter is used, and treatments of five to ten minutes with the light covering the whole affected area are given daily or every two days during periods of congestion.

The treatment with *beta-emanations of radium* which has been discussed on page 189 may prove to be of great value, as indicated by Woods' results in this condition and by 1 case of the author's.

Sodium salicylate internally seems of value in controlling inflammation during such periods and should be given in large doses, 120 grains a day for the average adult. While the tuberculous origin is insisted upon by most of those who have studied this condition, it is quite possible that other factors play a part in certain cases, so that definite foci of infection should not be neglected. While these cases are not common, their chronic course, usually with numerous recurrences until the vision is seriously compromised, justifies the most careful study of each case and the use of all measures which offer any promise of relief.

DENDRITIC KERATITIS.

Dendritic keratitis is now known to be *due to involvement of the cornea with the virus of herpes simplex* and to be identical in nature with herpes of the lip and genitalia. While herpetic lesions do not always assume the typical branching dendritic form, their identity is recognized by the fact that they are superficial and tend to spread rapidly over large areas of the cornea and by the corneal anesthesia usually present. On account of this anesthesia and the accompanying disturbance of nutrition of the epithelium, eyes with herpetic keratitis should be kept constantly covered. *The local application which is of most value here is iodine* and the concentrated solution previously described is a convenient form.* Applications should be made every day or every two days to the whole area which stains with fluorescein. Gun-

* See p. 247.

derson, from careful study of a large series of cases, concludes that destruction with iodine of all the epithelium containing the virus is always successful in stopping progress of the condition. In his hands, one complete application was usually successful. Progress of the ulceration occurred only when the application was incomplete. The author has found that phototherapy, in addition to the use of iodine, is of value in dendritic keratitis. The uviol light affords the safest method, eight to ten minutes daily being employed, but the Kromayer light with special applicators to limit its effect also may be employed, with 80 per cent erythema dose twice a week.

Where light treatment is not available, and the ulcer does not heal promptly on iodine, other antiseptics should be tried. In general, agents which cause necrosis, such as phenol and nitric acid, are not advised in herpetic keratitis, as the virus when not completely destroyed, seems to spread more rapidly in any tissues damaged by such chemical agents. Trichloracetic acid diluted to 50 per cent is often valuable, and a few obstinate cases have been seen to clear up promptly after one application of mercurochrome paste. (Mercurochrome crystals with a few drops of water added to make a paste.) The use of roentgen-rays has been warmly recommended by di Marzio, Berud and others. Twenty to 30 per cent of an erythema dose is advised by di Marzio, and since only one or two treatments are usually necessary, this may be given without danger to the eye. Berud gives only 8 per cent of an erythema dose, repeated four times. The author has seen apparently good results from one treatment of 30 per cent erythema dose in a number of obstinate cases.

Atropine is used in this condition, as in any other form of keratitis. Protein injections have been avoided, as the use of typhoid vaccines has in a very few instances been reported as the cause of herpetic keratitis. The effect of removing foci of infections on this condition is hard to explain unless we assume that the virus itself may be present in such foci

or that the resulting improvement in general condition is of value. Improvement has undoubtedly followed such removal, however, in a number of cases, so that foci should be looked for in obstinate or recurrent cases.

Paracentesis is only necessary in a few obstinate cases, and in these it should be performed at the limbus, as incision near the ulcer appears to allow involvement of the deeper layers of the cornea.

DISCIFORM KERATITIS.

Disciform keratitis, a non-luetic deep opacity of the central part of the cornea with marked thickening of the cornea *must be considered*, in view of the work of Grüter and others, *to be also caused by the herpes virus*, at least in the majority of cases. The beneficial effect of removing foci of infection in this condition, which has been frequently reported, must not be considered as certain proof of the etiological relationship of such foci, but only of their possible importance as secondary factors, as in the case of dendritic keratitis. Definite foci, when present, should be removed, as the condition is a serious one in which even secondary factors cannot be neglected. The possibility of tuberculosis must also be considered, as cases of keratitis profunda have been described which greatly resembled disciform keratitis, and which were considered undoubtedly tuberculous. If the tuberculin test is positive a course of tuberculin is indicated unless the lesion clears up under other measures.

Where congestion and pain are present atropine and large doses of the salicylates are of great value. The use of foreign protein injections is also indicated, and these should be made large enough to produce definite febrile reactions. Arsphenamine, potassium iodide and mercury have been frequently employed, with the idea of combating some unknown infection, but the evidence in favor of their use is not convincing.

Because of the known effect of ultraviolet light on the

herpes virus, treatment with the uviol light or a careful trial of roentgenotherapy would seem logical.

When the congestion has subsided, or in the cases where no congestion is present, an attempt to clear the resulting opacity by prolonged use of dionin and massage of the cornea with yellow oxide of mercury ointment is indicated. The patient can be taught to carry out the latter procedure, rubbing the closed lids over the cornea for thirty seconds twice a day after the ointment is introduced in the conjunctival sac.

SUPERFICIAL PUNCTATE KERATITIS.

The condition which was described by Fuchs has in recent years been shown to include, in all probability, a number of cases differing considerably from his original picture. In a typical case the *small infiltrates in the superficial layers of* the cornea are visible with the naked eye. In other cases, however, the chief signs are a marked conjunctival congestion with symptoms of irritation but nothing to be seen grossly in the cornea. Slit-lamp examination shows a multitude of very fine lines and dots in the corneal epithelium many of which stain with fluorescein. This condition has been apparently much more common in recent years and has been called in Germany "kerato-conjunctivitis epidemica." There is evidence that both the larger and smaller lesions are due to a virus perhaps allied to, but not identical with, the virus of herpes simplex. It is a self-limited condition, as a rule, but symptoms may persist for three weeks to three months and recurrences are not uncommon. Vision is interfered with slightly during the attack, but there is seldom any appreciable permanent visual defect.

Treatment is not very satisfactory. The larger lesions seem to heal more quickly if they are touched with a very fine cotton point dipped in trichloracetic acid or the saturated iodine solution. Treatment of the conjunctiva with strong astringents is painful and does not seem to be of much value.

Cowan has advised the instillation three or four times a day of 2 per cent *potassium iodide solution with two drops of compound iodine solution to the ounce.* In obstinate cases he employs cotton pledgets soaked in Pregl's iodine which are placed in the upper and lower cul-de-sac. The author has found the solution of potassium iodide as useful as anything in this condition but has hesitated to employ the iodine packs. Cycloplegia may relieve pain during more acute attacks and a 0.2 per cent solution of atropine is sufficiently active. If

FIG. 51.—Superficial punctate keratitis (marginal type).

only one eye is affected, it is best to keep it covered until healing is complete while when both eyes are involved this is impossible for practical reasons.

A group of cases described by Magitot as "subepithelial keratitis" was possibly of the same nature. These cases and a group described by Charlin were greatly relieved by *cocainization of the nasal mucosa.* Charlin found swelling of the turbinates on the affected side to be constant in his series, which be grouped as the "syndrome of the nasal nerve." The exact pathology involved is not clear but a nasal examination may be indicated in obstinate cases, followed by appropriate treatment of any nasal pathology which is found

EPITHELIAL DYSTROPHY OF THE CORNEA.

The typical condition described by Fuchs is exceedingly rare. It consists in marked edema of the corneal epithelium, with multiple epithelial defects, associated with hypotony and folds in Descement's membrane, the resulting opacities being sufficient to greatly reduce vision. The cause is unknown and no treatment is known to be of value. The author has described a *mild form of epithelial dystrophy*, in which the changes are confined to the epithelium and loss of vision is much less marked or inconsiderable. Before the routine use of the Schirmer test an apparent deficiency of lacrimation was noted in some such cases and it seems likely that these would now be classified as mild cases of keratoconjunctivitis sicca. In a few recent cases, however, the Schirmer test has shown normal lacrimation and such cases must apparently be considered as showing a dystrophy or nutritional defect of the corneal epithelium. It is important that the Schirmer test be employed in cases presenting such epithelial lesions as cases showing deficient lacrimation obtain marked relief from the treatment to be described for that condition.

In what may be called true cases of mild epithelial dystrophy, *considerable symptomatic relief is afforded by the use of dionin.*

It is used three to four times a day, beginning with the 1 per cent solution and increasing the concentration to 2 to 4 per cent according to the patient's tolerance and the relief obtained. In a certain number of cases, dionin is not well tolerated, and in these a weak local anesthetic, such as 1 per cent novocaine hydrochloride, is employed. Along with this, an *alkaline wash* is usually prescribed, to be instilled every two to three hours or oftener, since a more or less marked deficiency of tears is present in most cases. The author employs the *Alkaline Buffer Solution No. 1* previously described, but a *3 per cent solution of sodium bicarbonate* is

also valuable. No irritating antiseptics, especially silver nitrate, should be employed as these only aggravate the condition.

Since certain cases were found to have a definite deficiency of vitamin A in the diet and were greatly benefited when this was corrected, *administration of a vitamin A concentrate,* usually carotene or halibut-liver oil, *has been made a routine part of treatment.* In these later cases improvement in the appearance of the corneas has been much more definite and a number have maintained entire relief from symptoms without the use of dionin or a local anesthetic. Reasons have been given in Chapter III for considering that such cases may represent a mild form of xerosis due to a degree of avitaminosis too slight to produce other symptoms. The local use of carotene-in-oil has been tried in several cases of especial severity, but without apparent benefit, while the inconvenience caused by the oily solution was considerable.

In a few women showing symptoms of ovarian insufficiency associated with the menopause, the use of a potent ovarian extract has apparently proven of value.

KERATO-CONJUNCTIVITIS SICCA.

This condition, due to deficiency of lacrimal secretion, has been completely discussed by Sjögren and in America by Bruce. In the typical condition almost no tears are present, and the conjunctival sac contains shreds of ropy secretion. The conjunctiva is red, thickened, and a few follicles may be present. The cornea may be grossly normal or may have a slightly dull appearance, with small particles of secretion or loosened epithelium adhering to its surface. In a few cases, the appearance is that known as *filamentous keratitis,* in which fairly long threads of epithelium hang down from the cornea. With the slitlamp many fine epithelial defects are seen in all cases and these are most numerous in the exposed portion of the cornea. The condition occurs most frequently in patients with arthritis who show deficiency in the secretion of the

salivary glands as well, as indicated by dryness of the mouth, and inability to swallow dry foods without taking water. Sjögren has shown that the lacrimal nnd salivary glands, in such cases, have undergone marked atrophic changes. It is as yet uncertain whether this is the result of chronic infection or, as Sjögren is now inclined to believe, of a systemic degenerative disease affecting glands and joints.

While extreme cases are recognized without difficulty, milder forms are not uncommon, and for the detection of such cases a quantitative test of lacrimal function is necessary. de Roetth has established standards for the *Schirmer test*

FIG. 52.—Technique of Schirmer test.

which have made it of much practical value. Whatman No. 41 filter paper, as employed in most laboratories, is cut into strips 35 mm. long and 5 mm. wide. The upper 5 mm. is folded and the folded portion is placed over the edge of the lower lid at the junction of the outer third with the inner two-thirds. (See Fig. 52.) The patient may hold the lids open, winking as often as desired. The amount of paper wet by the tears is measured after five minutes. The test should be applied before any solutions have been used in the sac and without previous manipulation of the lids. In normal young adults the whole strip is usually moistened within three to five minutes. As age progresses the amount of lacrimation becomes less and after the age of forty, one-third of

normal persons show a relative deficiency, according to de Roetth, moistening less than 15 mm. after five minutes.* Only a certain proportion of such persons have symptoms of dryness and still fewer show epithelial defects of the cornea. It may be said, however, that in persons who moisten less than 15 mm. after five minutes and who have symptoms of conjunctival irritation, deficiency of tears may be suspected as the causative factor. In those who moisten 5 mm. or less it is quite likely to be the cause of symptoms. In typical cases of the Sjögren syndrome no moistening of the paper is usually observed.

Treatment.—*All antiseptics and astringents are to be avoided* when the diagnosis of kerato-conjunctivitis sicca is made, as such agents only increase the symptoms. This is true in the mild cases without complete absence of tears. The *use of a substitute for tears* gives great relief in the mild cases and the author has found Rucker's combination of 0.7 per cent gelatin in Locke's solution to be exceedingly useful. Three grains of chloretone to the ounce is added as a preservative. The solution is used five to ten times a day or as often as symptoms of dryness are noted. In typical cases, however, the best method of obtaining relief is *closure of the tear-points* as proposed by Beetham in 1935. This is done with the idea of retaining all moisture in the conjunctival sac. Closure of the lower tear-points alone gives considerable relief but Bruce has shown that results are much better when the upper tear-points are also closed. He destroys the epithelium of each canaliculus as far as the common canaliculus with the diathermy needle, but the author has found the use of trichloracetic acid to be quite effective. After dilatation of the tear-point, a fine applicator covered by a few threads of cotton dipped in pure trichloracetic acid is inserted for 3 to 4 mm. and turned about, the application being repeated after again moistening the applicator.

In cases retaining some lacrimal function, it is sometimes

* The folded 5 mm of the paper is disregarded

possible to increase the amount of tears secreted. Vitamin A in large doses has been of apparent value when a dietary deficiency was suspected, while the use of estrogenic extracts in women past the menopause has also given relief in some cases. The oral administration of pilocarpine, $\frac{1}{5}$ grain two or three times a day, or of prostigmine has caused a moderate increase of tears in a few cases.

The importance of recognizing this condition and of separating it from chronic conjunctivitis due to infection cannot be sufficiently stressed, as the therapeutic indications in the two conditions are diametrically opposed.

KERATITIS DUE TO LAGOPHTHALMOS.

Exposure of the cornea due to incomplete closure of the lids occurs after facial paralysis, in marked exophthalmos, and when the lids are held apart by scar tissue. The lower portion of the cornea which is exposed during sleep is always first affected and usually *before keratitis occurs there is a redness and hypertrophy of the lower bulbar conjunctiva. Whenever this occurs, the cornea must be protected,* as otherwise infection and necrosis of the cornea may result in loss of the globe or permanent corneal scarring.

In facial paralysis it may be sufficient to close the lids over the globe by a dressing worn at night. The palpebral fissure should be filled with sterile vaseline and oiled paper or smooth tissue should be placed so as to protect the cornea from contact with cotton or gauze in case the lids should come open. This and the use of a mild antiseptic several times a day in the conjunctival sac will often prevent keratitis. *In severe exophthalmos,* however, where the lids are never closed, *it is necessary to protect the cornea night and day.* For this purpose, a moist chamber of roentgen-ray film (see Fig. 43) is most useful.

When keratitis has already begun it *is often necessary to close the lids by a minor surgical procedure.* A partial blephar-

The treatment of *recurrent erosion of the cornea* is considered in Chapter XVI, since, although sometimes occurring spontaneously, it is usually due to a slight injury.

KERATITIS NEURO-PARALYTICA.

After section of the sensory root of the trigeminal nerve or alcohol injection of the ganglion, *certain precautions are necessary to avoid the development of keratitis.* In all such cases, although no symptoms may be noticed by the patient, and the corneæ may appear quite normal on gross examination, slit-lamp examination discloses edema of the epithelium and a number of microscopic areas which stain with fluorescein. Injury by a foreign body or unusual exposure to wind or dust under such conditions often gives rise to one or more larger erosions which easily become infected and may result in loss of the eye.

The most important measures of protection are *the use of a non-irritating solution in the conjunctival sac night and morning, and the wearing of protective glasses during exposure to wind and dust.* The solution must be employed most carefully. If a dropper is employed, it must not touch the cornea at any time, and perhaps the safest method is the use of cotton dipped in the solution and squeezed so that the solution drips into the conjunctival sac. Sterile normal saline or distilled water are the safest liquids for this purpose. No antiseptics should be employed in such cases, unless conjunctival infection is present. If it is necessary to employ cycloplegics for any reason, no crystals must be allowed to enter the conjunctival sac.

When erosions or areas of keratitis develop in such cases, the eye must be at once covered with a moist chamber, which is worn constantly until the lesion has healed. This is usually sufficient if the case is seen early. If a deep infection of the cornea is present, however, it must be treated by the methods described for serpent ulcer. Application of trichloracetic acid or optochin powder must be made most carefully, so as

here the intramuscular use of *sulpharsphenamine*, in doses of 0.2, 0.3 and 0.45 gm., has apparently been of almost equal value with arsphenamioe, which must be given by vein. The usual precautions when giving arsenicals should be observed. A course of eight to ten injections is given, repeated, after a suitable interval, as indicated by the condition. Mercury should also be given, usually at the same time as the arsenicals, and by inunction. The course of mercury and arsphenamine should be followed by postassium iodide, and after all inflammatory symptoms have subsided mercury and the iodides should be continued for at least a year, usually being used during alternate weeks, with a free week after two weeks of treatment. While it is undoubtedly safer to continue treatment until a negative Wassermann is obtained, this is often difficult in hereditary lues and in some cases apparently impossible. Many such "Wassermann-fast" patients have been watched for years without ever having shown any other symptoms of active lues after their interstitial keratitis. Such patients are often of a class not easy to follow, so that we must consider ourselves fortunate, in many cases, if we are able to keep them under treatment as outlined above for a year or until the danger of active recurrence is fairly well past. One should lose no time at the outset in deciding which patients will carry out the inunctions properly, and which will do better if given intramuscular injections of mercury, salicylate or bismuth. The author has seen no superiority in the latter drug over mercury, though many syphilographers claim that a change to bismuth affects the serological reaction favorably where this remains strongly positive.

It would seem superfluous, perhaps, to speak of foreign protein injections in this condition for which we have specific methods of treatment. It is a fact, however, that a fair number of cases do not respond to specific treatment favorably and show a persistence of severe inflammatory symptoms and increasing corneal opacity in spite of it. *In these cases*, as was pointed out by Marchesani and others, *foreign*

on the clearing of corneal scars following injections of wintergreen oil into the cornea have not as yet been confirmed by other observers.

It must be emphasized that, though the course of interstitial keratitis is a long one, the first days after its onset is the important time for therapy, and a few days lost at that period may be the cause of irreparable damage to vision. In a typical case no time should be lost while waiting for a Wassermann report, but active treatment should be commenced at once.

When, after clearing of the scar has become stationary, vision remains considerably reduced, *an attempt to improve vision by keratoplasty may be considered.* It is in this condition, in which a certain amount of clear peripheral cornea exists, that the most brilliant results of this operation are obtained.

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CHAPTER IX.

DISEASES OF THE UVEAL TRACT.

CAUSES OF UVEITIS.

With what we now know about uveitis, *our treatment may in most cases be directed at the cause,* or at the most likely of several possible causes. Thus the most important step is a prompt search for all possible causes, and a prompt decision as to which one shall be attacked. It is in this condition, especially that so much time is often lost in waiting for one laboratory report after the other, and that the use of group clinic facilities, or the equivalent in association with one's various colleagues, is absolutely necessary. A blood Wassermann, examination of the nose and throat, roentgen-rays of the teeth and of the sinuses where nasal examination indicates it, will be necessary in most cases of uveitis, and these should all be carried out, where possible, on the day when the patient is first seen There is still, in the minds of some ophthalmologists, a fear of removing foci of infection during an acute attack of uveitis, but this is not justified, in the author's opinion. While removal of infected tonsils may precipitate an increase of inflammatory symptoms which may even be alarming, this is the exception, and such flare-ups almost never cause permanent damage to the eye. The usual effect of such removal, provided the proper focus is removed, is a relief of inflammation so prompt and complete as to appear miraculous, and *such relief should be given at the earliest possible moment.* The same kind of relief is often afforded by one or two injections of neoarsphenamine in luetic iritis, accompanied by other treatment.

The question of whether this or that pair of tonsils should be removed, or whether a tooth should be extracted first, will often require much judgment, but it must be assumed that every case of uveitis has a cause, and that even if the

acute attack is aborted by local treatment recurrences are to be expected unless the cause is found. Where the above examinations furnish no definite information the genito-urinary tract should be thoroughly investigated, even if there is no history of gonorrhea, since it is now recognized that non-gonorrheal prostatitis and seminal vesiculitis are not uncommon and may cause uveitis. A tuberculin test will also be indicated and a careful general examination with special reference to the intestinal tract.

Where the Wassermann is positive other possible sources of infection may usually be ignored until the effect of vigorous antiluetic treatment has been ascertained. The relative importance of various causes varies with different reports, but nearly all observers agree that lues is one of the commonest causes of acute iritis, accounting for 20 to 25 per cent of cases. Next in importance as a cause of acute uveitis is probably the tonsils in young adults, and dental sepsis and sinusitis in older persons. In the chronic forms of uveitis tuberculosis assumes a much greater importance, accounting for from 10 to 40 per cent of cases. Gonorrhea causes a number of especially severe cases of acute iritis, and although prostatic massage and instillations may provoke temporary exacerbations of inflammation, continuance of such treatment usually gives relief. In some obstinate cases vesiculectomy or direct injections into the vesicles may be necessary.

Where removal of a tooth or a pair of tonsils does not give relief within a few days, in acute cases, no time should be lost in searching further. Something which is especially easy to overlook is the presence of retained infected dental roots or infected areas of bone in mouths from which all the teeth are said to have been removed. The author has been guilty of this, with exceedingly serious results, in at least one case which was later found to have an osteomyelitis of the superior maxilla requiring complete alveolectomy. Many such cases are not relieved by simple extraction of the teeth, and a careful study of satisfactory dental roentgen-rays will

importance of this in avoiding permanent posterior synechiæ demands an early diagnosis of the existence of iritis, and here the exact information furnished by the slit-lamp may be of inestimable value. For many mild cases are still seen which have been given treatment for conjunctivitis until slit-lamp examination reveals an anterior chamber full of cells. As soon as the diagnosis is made, 1 per cent *atropine in solution or ointment should be used rigorously enough to obtain mydriasis*, and this should be maintained by frequent instillations, 5 or 10 drops of the 1 per cent solution, three times a day, being necessary in a moderately severe case. Where a 1 per cent solution fails to dilate the pupil stronger solutions or a few grains of the powder dusted in the sac may be successful. Apparently of more value is the *subconjunctival injection of atropine.* If cocaine and adrenalin are added to the solution a summation of effect by simultaneously stimulating the dilator and paralyzing the sphincter is obtained. The mixture of 2 minims each of 2 per cent atropine, 2 per cent cocaine and 1 to 1000 adrenalin (Suker), injected subconjunctivally, is often effective in severe cases. Rodin recommends *injections of atropine and adrenalin* only, using in his last reported cases 2 minims of 2 per cent atropine and 4 minims of 1 to 1000 adrenalin divided in two injections above and below the limbus. Concentrated solutions of epinephrine, which will be discussed further in considering glaucoma, are now frequently used for this purpose, to break up synechiæ already formed. As previously stated (page 57) the 10 per cent emulsion of neosynephrin is very effective for this purpose. These measures should, however, be preceded and followed by atropine, and even then, unless the cause of inflammation has been removed or treated, the pupil will only too often return to its original size the day following dilatation by epinephrine. In giving atropine it must be remembered that absorption is chiefly through the cornea, and so instillation is best given with the patient lying down, the lids being held open so that the cornea is flooded by the solution. The previous use of 2 per cent

chapters. In acute iridocyclitis due to lues, vigorous antiluetic treatment usually affords dramatic relief. When due to other causes, the intravenous injection of 30 to 50 million killed typhoid hacilli, followed by adequate doses of sulfanilamide or sodium salicylate will often produce results almost as striking. The relative advantages of the sulfonamides and the salicylates have been discussed and the choice of a drug will depend upon the type of infection assumed to be present and upon the reaction of the patient. Dosage may be cut down when relief is obtained but the drug should not be stopped until the signs of active inflammation have subsided. The comhination of foreign protein therapy with medication presents no special dangers and is often superior to the use of chemotherapy alone, but when the response to a drug is satisfactory tbe additional discomfort of foreign protein shocks may in many cases be avoided. The use of high temperatures produced by diathermy or cahinets is seldom necessary in iridocyclitis, although good results bave been reported with the metbod.

SYMPATHETIC OPHTHALMIA.

Sympathetic ophthalmia is a form of uveitis which must be considered by itself. A few words as to its etiology are necessary, since the reports of Alan Woods on the use of uveal pigment in antigen in treating the disease are hased upon the anaphylactic theory of its origin. The various theories have been thoroughly discussed by H. Gifford, in 1926, and more hriefly by the author, in 1929. In spite of the tendency in this country to accept the anaphylactic theory, because of the work of Woods and others, the conclusion was drawn that it fails to offer an acceptable explanation of several essential phenomena of the disease, such as the occurrence of optic neuritis in the second eye, the occurrence of the disease almost exclusively after a penetrating wound and not after endogenous iritis, which should

present the same causal conditions according to the anaphylactic theory, and the beneficial effect of enucleating the injured eye. It was concluded that *most of the known facts are best explained by assuming the introduction of some living organism in the first eye, which reaches the second eye either by the blood stream or through the optic nerves and chiasm.* This organism or group of organisms may be a bacterium as yet undiscovered, or a filterable virus, such as the herpes virus. The eye first affected must then be considered a focus of infection. Its early removal may allow the pathogenic agent which has already reached the second eye to be destroyed there. Failure of the process to subside would indicate that a secondary process has been set up in that eye which its defensive mechanism is unable to overcome.

The first thing to be considered in the treatment of sympathetic ophthalmia is its **prophylaxis.** Prompt enucleation of eyes following severe injuries rendering the prospect of vision hopeless undoubtedly prevents many cases, and would prevent more if we could overcome the almost superstitious faith with which some people cling to a sightless and ugly stump which they are pleased to call an eye. When the injured eye retains vision we are faced with a decision whether or not keeping it involves the danger of sympathetic ophthalmia. Generally the larger the wound, especially if it involves the ciliary body with prolapse of uveal tissue, the greater the danger of sympathetic ophthalmia. One is sometimes surprised, however, at the way in which wounds will heal without complications with retention of useful vision, and where useful vision is present it is usually best to make some effort to save the eye. In the case of children, however, or persons living at a distance from competent surveillance, one is undoubtedly inclined to err on the side of safety and remove a number of eyes which might be saved under more favorable circumstances.

Where sympathetic ophthalmia is already present it is generally recognized that simple enucleation is the safest pro-

cedure. Where the operation is done early, however, with no signs of sympathetic ophthalmia present, there can be no doubt that some of its substitutes are to be preferred for their cosmetic result and would be more often employed if there were not some evidence that they involve a slightly greater risk of later sympathetic ophthalmia than simple enucleation. Although sympathetic ophthalmia has occurred in a number of cases after enucleation (80 cases, according to Schieck) as well as evisceration, and the statistics reported are insufficient for definite judgment, they do indicate a slightly greater risk following evisceration and evisceration with gold-ball implantation, and H. Gifford concludes that where sympathetic ophthalmia is much to be feared enucleation is probably safer. However, in a fresh injury, before sympathetic inflammation has begun, especially in young persons, the risk is so slight that simple evisceration is justified for the sake of the better stump obtained. Certainly where panophthalmitis has developed evisceration is the operation of choice, as here the chance of sympathetic ophthalmia is very slight in any case.

When an attempt to keep the eye has been decided upon the most important measure is *the prompt covering of any wound containing prolapsed uveal tissue with a sliding conjunctival flap.* A detail which may seem trivial, but which the author has seen neglected with disastrous results, is the careful preparation of the flap and placing of sutures ready to tie before excising the prolapse. This excision is often followed by loss of vitreous which is reduced to a minimum if the flap is ready to close. Another detail which may help to avoid loss of vitreous is the use of van Lint akinesia, as for a cataract operation, before any operative procedure is begun. It is more necessary here than in the cataract operation because our patients are more likely to squeeze, and we are more apt to meet with vitreous prolapse. Another important prophylactic measure is *the use of a foreign protein injection as soon as possible after the time of injury.* In

definite evidence of inflammation in the second eye, must be prepared to combat it with every means in our power. There can be no hesitation in removing the sympathogenic eye if it is blind or nearly so. If it still has useful vision, especially if the condition of the second eye is already almost as bad as that of the first eye, an effort may be made to save the first eye, as cases have been reported in which it became the only useful one. The all-important thing is to act promptly when enucleation is decided upon, as the delay of a day or two may mean a great difference in the outcome.

The *use of large doses of sodium salicylate* has become almost a standard method of treatment, since H. Gifford published his results with it in 1899, and his dose of 1 grain per day for every pound of body weight of the patient has been accepted by many. It should be remembered, however, that much larger doses are tolerated by the average patient, so that where this dosage is not producing results it should be increased to 200 or 250 grains a day for an adult.

It is especially important not to stop the salicylates as soon as the eye becomes quiet, but to taper off gradually and continue some salicylates or their substitutes, 60 to 90 grains a day, for weeks or months longer. These amounts can be borne by nearly all patients without any ill-effects except the discomfort of taking them.

The results with sulfanilamide previously mentioned, although few, are encouraging to further use of the drug in sympathetic ophthalmia. The author has seen at least 2 cases in which the results of sulfanilamide were remarkably good, and it may he justified to try this drug first in preference to sodium salicylate. Certainly it should he tried in full dosage in cases which do not respond to the salicylates and foreign protein.

Foreign protein therapy has been used in various forms, and especial enthusiasm has been shown recently for injections of autoserum by Vila Coro and of antidiphtheritic serum hy Verhoeff, who used very large doses. The author

has never been persuaded that autoserum acts in any other way than as a protein injection, and hence has preferred milk or typhoid vaccines. With the latter one can be more certain of the action desired, as Allen has shown. The salicylates should be stopped for twenty-four hours after a foreign protein injection, to allow a proper reaction.

What part focal infections can play in sympathetic ophthalmia is hard to understand, unless germs or toxins from such a focus can accumulate in the diseased organ and complicate the disease already present. A number of cases have been reported, however, in which removal of such foci was apparently of benefit.

In treating the complications of sympathetic ophthalmia, such as glaucoma and cataract, one is faced with the well-known tendency of eyes with sympathetic ophthalmia to respond to any operative interference by increased inflammation which may cause destruction of the eye. An iridectomy for glaucoma under these circumstances is apt to result disastrously, and probably the mildest form of interference when the iris is bulging is a small peripheral iridotomy performed by cutting through the iris root with a thin Graefe knife or Knapp needle, bringing the knife out through the sclera under the conjunctiva. In several cases the author has been able to keep the tension down by ergotamine, given subcutaneously, until the inflammation was under control. In other cases, one or more paracenteses have accomplished the same result. In these cases one must do something when the tension remains high, but *in the case of cataract one can and should wait until the eye has been quiet for at least a year before attempting any operation.* Even then, one should be especially certain that no foci of infection are present and should have the patient well salicylized before operating.

CHOROIDITIS.

Here, where the anterior segment is not involved, there is little to be accomplished by local treatment, and *our main concern is in locating and treating some general cause for the*

condition. The factors to be considered and the diagnostic procedures to be carried out are the same as for iridocyclitis. Where tuberculosis is suspected, the tuberculin tests must be carried out with the utmost care to avoid a focal reaction. The intradermal test with solution Nos. 3 and 4 should first be done and solution Nos. 1 and 2 used only if the other two are negative. (See Chapter IV.) Treatment with tuberculin must also be especially cautious, the dosage being increased more slowly than is done in iritis. Atropine is usually used with the idea of putting the ciliary muscle at rest, and so lessening congestion of the uveal tract. Only a small amount of atropine need be used, and since the benefits of its use are none too certain, it may be dispensed with in some cases where the patient must continue his occupation. While usually not so dramatic in onset as iritis, the dangers of permanent damage to vision, especially if the lesion is near the macula, demand that no time be lost in locating the source of infection. Lues is as important a factor here as in iritis, and the results of prompt and vigorous antiluetic treatment are as satisfactory.

Foci of infection must be dealt with in the same way, and *effort to find such foci must not cease as long as any active areas of choroiditis are to be seen in the fundus.* The salicylates and foreign proteins are also important adjuncts in the treatment of choroiditis. Subconjunctival injections of hypertonic saline are advised by many ophthalmologists, with the idea of absorbing toxic substances and even opacities by osmosis, but there is much question whether they have any such effect, and the pain attending their use is often quite severe. Sweats with pilocarpine, $\frac{1}{7}$ to $\frac{1}{5}$ grain, injected subcutaneously, are advised for the same reason. These have no disadvantages except in debilitated persons, and may always be tried. When the salicylates are being used the diaphoresis produced may be made as vigorous as that from pilocarpine by giving a double dose (60 grains), after which extra blankets and hot-water bags are applied. Thirty to 45 grains in some persons will produce satisfactory sweating. The use of potassium

It will be understood that what has been said of the last group of possible causes for uveitis will apply to only a few cases. Attention will be directed in most cases to one of the usual causes, syphilis, tuberculosis and the foci of infection first mentioned, and in the presence of evidence for any of these, in which a positive tuberculin test must be considered exceedingly important, other causes not so likely will require serious consideration only when treatment of the more common causes has failed.

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covered early so that proper management may prepare the patient for eventual cataract extraction.

The possibility that *dietary deficiencies* may have some relation to senile cataract has aroused some interest in recent years, due to biochemical studies on the lens. The work of Muller and Buschke, Bietti, Bellows and others has shown that vitamin C is present in the normal lens and aqueous in large amounts. It is absent from the cataractous lens and from the aqueous of eyes from which the lens has been removed. Vitamin C and glutathione, a polypetide containing sulphur, are the substances chiefly responsible for maintaining active interchange of oxygen and hydrogen in the lens. While it is difficult to produce cataract in animals deprived of vitamin C before fatal scurvy intervenes, this has been done under certain circumstances. The question is a complicated one, and it is possible that absence of vitamin C in the cataractous lens is merely a result of the cataractous process. The same may be said of riboflavin, or vitamin G, absence of which does cause cataract in experimental animals. (See page 83.)

That the course of senile cataract may be influenced by the use of vitamin C must be considered at this time as only an interesting possibility. *The statement of Josephson that lens opacities improve under such treatment was not supported by convincing evidence, and has not been substantiated.* Bellows* administered vitamin C in large amounts to patients with incipient cataract but observed no change in vision or in the appearance of the opacities. It would seem reasonable, however, in early cases of cataract, to insure a proper supply of vitamins B and C in the diet, with the idea that progress of the lens opacities might conceivably be delayed or prevented.

Local therapy has included the use of potassium iodide in 2.5 and 5 per cent solution in an eye-bath, or by instillation (Badal), by subconjunctival injection, or combined with iontophoresis (Angelucci). The evidence offered for these methods is unconvincing, and reports of improvement or the

* Personal communication.

was maintained for several years. He gives a single injection of 20 minims of 1 to 5000 mercuric cyanide solution subconjunctivally, the dose being divided between the upper and lower bulbar conjunctiva near the equator. This must be preceded by local cocainization and usually by morphine, as the pain for an hour or so afterwards may be severe. A very severe chemosis results, with such swelling of the lids that the eye often remains shut for twenty-four hours, and which requires a week or longer for complete resolution. Only one injection is usually given, but in later cases Dean has followed this with instillations of dionin. There is the same justification for this procedure in suitable cases as for the use of dionin, except that the inconvenience to the patient is much more serious.

Glandular therapy was based on numerous observations of lamellar cataract in children with tetany and rickets. At first thyroid extract was employed, but when it became known that tetany was due to parathyroid deficiency, extracts of the parathyroid and recently, the newly isolated substance parathormone were employed, in addition to calcium. Since it is established that the use of parathyroid extract combined with calcium will prevent the occurrence of tetany in definite cases of postoperative tetany parathyroideopriva, it seems logical that the same effect may be exerted on the occurrence of lens opacities from the same cause. Of such cases which have already shown cataract only a few have been given parathyroid extract in various forms, and the fact that no effect was observed on the progress of the opacities is not surprising, since the condition may be supposed to have been too far advanced when treatment was begun. Once a considerable amount of lens opacity has developed, any actual clearing of this would not be expected. Certainly in cases of juvenile cataract with other evidences of glandular imbalance, the blood calcium should be tested, and if it is definitely low this should be an indication for parathyroid and calcium therapy if the condition is not too far advanced.

opacities. Why only the opacities should be absorbed and not the whole lens, he does not explain, and his case reports are no more convincing than those put forward in support of many other methods of treating cataract. Not only is there no theoretical reason to expect results from such treatment, but the injections produce definite systemic disturbances, and it has even been stated that patients who have undergone such therapy show reactions much more severe than normal at the time of their operation for cataract Ellis recently observed a number of patients treated by this method and was unable to note any difference in their course from that of a similar series of untreated cases.

The use of small exposures to radium, as formerly advocated by Martin Cohen, Franklin and Cordes and others, has not found many advocates, and besides the lack of any apparent reason for its use, cannot be considered free from the danger of actually increasing lens opacities.

Certainly the best thing we can do for the patient with incipient cataract is careful and repeated refraction, as changes, especially in the strength and axis of cylinder required, are constantly occurring during the course of cataract. Distal telescopic glasses will allow a few persons to read who would otherwise be incapable of doing so, when it is desirable to postpone operation. On account of the necessity for great care in choosing these glasses, in adjusting them and keeping them in adjustment, disappointments in their use are not uncommon, and elderly persons often obtain more practical benefit from one of the stationary magnifying devices especially arranged for reading. A simple device for this purpose is the so-called reading crystal, a block of glass with convex top, the thickness of the glass corresponding to the focal length of its lenticular power. When this is placed on a flat surface a line of print, 2 inches long, is seen in good focus, with a magnification of about 4 diameters. A modification of this, called the "Electrolens," incorporates a light focussed on the reading surface.*

* Made by the American Optical Company.

be recorded accurately. A tonometric record of every cataract patient at each visit is certainly the safest procedure and will save the ophthalmologist some unpleasant surprises.

The indications for operation may be briefly considered. The safest time is certainly when the cataract is mature, and the fact that the other eye still has useful vision should not cause us to postpone operation beyond this time, unless, on account of advanced age or other general conditions, it is believed the better eye will outlast the patient. In bilateral nuclear sclerosis it is impractical to wait for either cataract to become mature, since this would permit the patient to be practically incapacitated for years. *It is better to operate on the more-advanced cataract as soon as vision in the other eye is sufficiently reduced to considerably limit the patient's activities.* Whether preliminary iridectomy will be done in such cases will depend on the individual case and on the training of the operator. In sclerosis of the lens or the various degrees of brown cataract a preliminary discission is seldom necessary, as little cortex is usually left. In immature cortical cataract a preliminary discission may be advisable. For those surgeons who have mastered a method of intracapsular extraction, this procedure need not be considered, and extraction may be performed whenever visual disability indicates it.

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days. Gradle has shown the importance of recording tension before and after the use of a cycloplegic, as by this means a certain number of patients was found whose tension was normal but who showed a pathological rise of tension under cycloplegia which justified the diagnosis of a pre-glaucomatous condition or even of glaucoma.

A general examination of the patient with chronic simple glaucoma is indicated, although in most cases very little will be found which has a direct influence on the intraocular tension. Search for foci of infection is of much less importance here than in inflammatory conditions such as uveitis, and only frank foci such as apical abscesses which involve in themselves a danger to health will require intervention. Such intervention is seldom followed by any reduction in intraocular tension and there is no reason for advising surgical intervention on "suspicious" tonsils or sinuses in cases of chronic simple glaucoma. Vascular hypertension may require medical care, but here again one will not expect much effect on the ocular condition as a result of such measures, which must rather be considered as a part of the preparation for possible operation.

A *record of blood chemistry* may be of value in view of recent work on the pathogenesis of edema. It has been shown by the work of Barker and others that in edema the sodium ion as provided by sodium chloride is an important factor in causing water to be retained in the tissues. In some patients with chronic glaucoma, a high carbon dioxide combining power of the blood, with a slight decrease in blood chlorides, indicating their retention in the tissues, is present. When such patients have a tension only slightly above normal it is sometimes possible to reduce this to normal by regulating the body chemistry. The same method is followed as is employed in patients with edema, which often causes the water-logged tissues of these latter patients to give up water in a most dramatic manner. *Sodium chloride is eliminated from the diet* as well as sodium in the form of baking soda or

case of simple glaucoma such treatment will produce a considerable fall in tension and will often keep it within normal limits for a considerable period. Miotics should be used often enough to maintain normal tension, if this is possible, or to ascertain how low it can be kept by their means. On account of the occasional occurrence of synechiæ after prolonged miosis pupils which remain very small should be allowed to return to normal size occasionally, and if they do not dilate freely after twenty-four hours without the drug they should be aided by a drop of homatropine or cocaine, the patient being watched carefully after this until the pupil is again under a miotic. When the pupils remain in extreme miosis as the result of a miotic, and still the tension is not brought down to normal, there seems little to be gained by increasing the strength of the drug, and other measures must not be delayed.

Patients who have been using a miotic for long periods often develop an *idiosyncrasy* to the drug employed. This *is especially common with eserine but also occurs with pilocarpine.* Hence signs of conjunctivitis and the symptom of itching must be watched for, and are indications for a change from eserine to pilocarpine or the reverse. When a patient has become sensitive to both drugs, the use of 3 per cent prostigmine bromide or 0.75 per cent carbaminoyl-cholin (doryl) may be useful.

The combination of 3 per cent prostigmine with 10 per cent mecholyl, as advised by Clarke, or of 1 per cent pilocarpine with 0.2 to 0.5 per cent eserine, producing synergism by affecting the neuromuscular arc at two different points, offers theoretical advantages over use of either drug alone and may preserve a somewhat lower tension. The author's experience with mecholyl and prostigmine in chronic glaucoma has, however, shown no very definite advantages over the use of eserine alone. It is the rule in a number of clinics that cases of chronic simple glaucoma in which the tension cannot be kept normal by 1 per cent pilocarpine should be

submitted to surgery without delay. This rule undoubtedly prevents loss of vision in many cases and may in general prove a useful one. There are some cases, however, in which operation must be delayed and a few in which a slightly more powerful miotic is tolerated while preserving normal tension.

The great danger of miotics is that of overconfidence in their effect, so that the vision and especially the fields as well as the tension should be watched carefully during their use. The use of a tension chart by which the patient's progress on various forms of treatment may be seen at a glance, is exceedingly convenient. The observation of Thiel, now amply confirmed by others, should be remembered, namely, that there is a characteristic daily curve of intraocular tension in glaucoma patients, tension usually but not always being highest on arising in the morning and lowest at night. Hence, it should be recorded in the morning when possible, and when the field is failing, even if our tonometric findings are normal, it must be considered that a rise of tension probably exists at some time of the day or night, or at least a tension too high for the lamina cribrosa of the particular patient. In these cases, and the more common ones where miotics exert their effect only for a time and then fail to have any effect, something else must be done.

When we were able to accept the pathogenesis of simple glaucoma as a blocking of the angle of the anterior chamber, it was logical to limit our ideas of medicinal therapy to miotics which were to free the iris root. Modern investigation, however, has made it necessary to consider other factors as of equal, if not greater importance. Such factors are the permeability of the capillaries, the nervous control of the intraocular vessels, the osmotic pressure of the blood and its chemical composition, and the possible effects of hormones from the ductless glands circulating in the blood. All these factors influence the amount of the intraocular fluids, which must be considered as formed by dialysis from the blood

serum of the capillaries.* Knowledge of these factors has suggested a number of additions to our therapy of glaucoma, a few of which have proven of definite value.

It must still be recognized that *in most patients whose tension cannot be controlled by miotics and the correction of definite pathology elsewhere in the body operation had best be undertaken at once.* There are certain conditions, however, which may make a delay advisable, or may even make operation impossible, and under such conditions the use of these newer therapeutic measures may prove of great value.

Some of these conditions are the following: In very advanced age or feeble health, in patients who have lost the sight of one eye, especially after operation, and with the fields cut down close to the fixation point in the remaining eye, and in patients who refuse operation. These conditions not infrequently apply in simple glaucoma. Another condition which may be mentioned here is met in secondary glaucoma, especially during sympathetic ophthalmia, where any operation may result in an access of inflammation.

Undoubtedly *the most useful of these modern methods of reducing tension is the use of epinephrin and its derivatives.* While the use of epinephrin in glaucoma is based on earlier experimental work by Wessely, A. Knapp and others, it has become widely known chiefly through the work of Hamburger in 1923 and his thirteen or more publications on the subject since that time. It was found that 1 to 1000 adrenalin was only effective by instillation in a small number of patients, but that on subconjunctival injection a marked mydriasis occurred which was followed by a fall of tension in most patients. This was first explained as due to vasoconstriction of the vascular uveal coat, the loss of blood producing a reduction in the volume of the intraocular contents. Since the maximal effect was noted twelve to twenty-four hours after the treatment, long after the vasoconstric-

* Recent evidence in favor of the secretory theory need not be discussed here

bitartrate in such an amount that 2.5 cc. of distilled water added to an ampoule gives a 2 per cent solution. This has been found to have an effect practically the same as that of lævoglaukosan. A 1 per cent solution of epinephrin hydrochloride is also now available for instillation in the same manner. The use of 10 per cent emulsion of neosynephrine by instillation has a similar effect.

Gradle showed that 1 to 1000 epinephrin produced an effect equal to that of subconjunctival injection when 4 to 5 minims were dropped on a small cotton pledget which was placed in the upper cul-de-sac and left there four minutes. Enough absorption occurs when it is used this way to give the local effect with no systemic symptoms. The method is simple, sufficient anesthesia being obtained by 1 or 2 drops of 2 per cent butyn, while with injections anesthesia must be more thorough. Apparently all three of these methods, injections of epinephrin, epinephrin packs and instillation of lævoglaukosan have practically the same effect on tension. Gredstedt, comparing injections of epinephrin with instillation of lævoglaukosan, found the effect of injection to be more marked and prolonged, while Hamburger prefers lævoglaukosan. Vannas has made an accurate record of the effects of epinephrin injections in 61 eyes and found that the reduction of tension usually lasted from two to three days. In the author's series of 50 cases in which packs and injections were used an appreciable reduction of tension occurred in most cases, the tension reaching below 25 mm. Schiotz in 42 cases. The average decrease of tension was 10 mm., falls of 20, 23 and 24 mm. being seen in certain cases. (See Fig. 54) All were cases in which miotics were being used but were not successful in maintaining normal tension. Miotics were continued after the treatments, and in 13 cases tension was kept within normal limits for one week or more, while in 5 the period was longer than a month. A number of these cases were kept under control by several such treatments for eight to twelve months, vision remaining the same as before

the treatments were commenced. In many cases later treatments were not so effective as the first one, and most cases finally required operation. Marked differences were observed in the response of individual cases to epinephrin, and where a first treatment is ineffective nothing is to be gained, usually, by further attempts.

Apparently the only complication resulting from treatment with epinephrin or glaukosan in simple glaucoma, which occurred in 2 of the author's cases, is an acute rise of tension

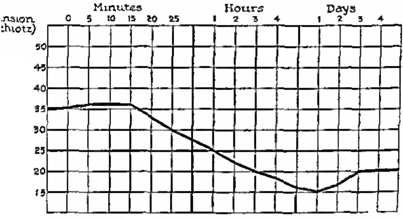

Fig 54 —Effect of epinephrin pack on intraocular tension in chronic simple glaucoma.

immediately following the treatment. This is apparently due to the accompanying mydriasis, as a slight initial rise of tension occurs in many cases during the period of mydriasis. Apparently this increase of tension in some cases is accompanied by actual blocking of the chamber angle, so that the tension continues to rise until an acute attack of glaucoma is precipitated. This has been reported in only a few cases of simple glaucoma, and in nearly all such cases it has been controlled by miotics without permanent damage to vision. In a few paracentesis has been necessary, or even iridectomy. *Such attacks may be prevented in the great*

majority of cases by using miotics vigorously enough before and after treatment to prevent or minimize the mydriasis, which in no way lessens the later effect of the treatment on tension, and this precaution should always be taken when epinephrin or glaukosan is used. 0.2 per cent eserine should be used twice every twenty minutes in the first hour afterwards and every half-hour for the next two hours, or often enough to keep the pupil small. The danger of acute rise of tension seems to be over in six to eight hours. It is the necessity of watching for these occasional acute attacks which make it seem inadvisable to prescribe epinephrin for use by the patient in ointment form, as has been recommended by Thiel.

There is still some difference of opinion as to the type of case in which adrenalin is indicated. *Most observers agree that it is ineffective in absolute, acute and hemorrhagic glaucoma.* In the last two conditions it is not only ineffective, but also dangerous, and should never be used. While some observers still advise it in secondary glaucoma and iritis glaucomatosa, where it was enthusiastically recommended on account of the simultaneous dilatation of the pupil and lowering of tension, others have seen disappointing results. Vannas reported an acute rise of tension in 3 such cases and no effect in 2 others. The author observed 2 such acute attacks, 1 of which necessitated enucleation of a previously blind eye, and most of the cases which showed no effect were of this type. Hence he believes Vannas' conclusion must be accepted, that epinephrin is contraindicated in types of glaucoma accompanied by any inflammation, and should be reserved for chronic simple glaucoma. (Its use as a mydriatic in iritis is, of course, not included in this statement and the condition of glaucoma following cataract extraction, which will be discussed later, constitutes another exception.)

Besides the miotics and epinephrin, which are used for their local effect, a group of drugs has been advised which are administered by mouth, or by injection, their effect being

explained as due to a decrease in capillary permeability or to constriction of the capillary bed. Such drugs are ergotamine, pituitrin and various calcium preparations.

Ergotamine, sold by the trade-name gynergen, because of its use in obstetrics, is a derivative of ergot. Besides causing contraction of the uterus, it raises the blood-pressure and depresses the end-organs of the sympathetic nervous system. Its use in glaucoma is based on the idea that increased tension is due to hyperactivity of the sympathetic system, and that such a drug would decrease the permeability of the vessels. It is dispensed in ampoules, $\frac{1}{2}$ ampoule containing the usual dose of $\frac{1}{250}$ grain for injection and in tablets of $\frac{1}{60}$ grain for oral use. Reports by Thiel, Heim and others covering a fairly large number of cases indicate that in simple glaucoma the tension could be kept normal for long periods by two daily injections or by oral doses of 2 or 3 tablets, two or three times a day. The author's experience with the drug has been chiefly in the types of glaucoma to be discussed later. In simple glaucoma some decrease in tension could be produced in certain cases, but since subcutaneous injections were impractical for any but hospital cases, and oral administration appeared to be less effective, it was not used in many cases. The expense of a drug which must be used in such large amounts is another important reason for preferring other measures in chronic simple glaucoma.

The use of **pituitrin** in chronic glaucoma was begun on the basis of Krogh's observation that it increased the tone of the vessels without the secondary vasodilatation produced by adrenalin. Samojloff found that subconjunctival injections of 0.3 to 0.5 cc. of the ordinary obstetrical preparation produced a marked fall of tension without dilatation of the pupil. No preliminary rise of tension such as is seen with adrenalin was ever observed. The decrease of tension was most marked on the second or third day after injection, and tension remained low for several days longer without the

use of miotics. With miotics tension was kept normal in a small number of cases for several weeks. No reports of this treatment have appeared in America, apparently. For further discussion of these substances and their place in the group of parasympathomimetic drugs see pages 52 and 53. The possible effect of certain electrolytes, especially calcium, strontium and barium in increasing the tone of the intraocular muscles is also discussed. (Page 53.)

In general, it may be said that *the effect of any of these methods aside from miotics is a temporary one and is of value in simple glaucoma chiefly in cases where operation must be delayed.* The danger inherent in their use is that operation will be delayed too long. This is often the result of overconfidence of patients in their effectiveness, allowing them to remain away from observation until irreparable damage to vision has occurred. They should not be used without the full understanding of the patient that constant observation is necessary during their use, and patients with chronic glaucoma should always be prepared for the necessity of an operation. There is always a tendency to delay a procedure involving any risk to vision, and it is certainly true that operations for glaucoma are delayed too long by too many ophthalmologists. Hence it seems well to repeat that *in any case where tension cannot be controlled by miotics or by a short trial of any of the above methods operation should be urged at once.*

Which operation shall be chosen will depend on the experience of the surgeon. There is fairly general agreement that iridectomy is not usually advisable in chronic simple glaucoma, but that one of the filtering operations, corneoscleral trephining, sclerectoiridectomy according to Lagrange, or iridencleisis according to Holth, is necessary. Iridencleisis with running conjunctival suture has, in the author's opinion, special indications in cases with the field cut down close to the fixation-point, as the anterior chamber fills more rapidly and marked hypotony occurs much less often than after

concentration of the blood plasma following such losses of water from the body, the concentrated plasma then replacing its fluid from the tissues, including the intraocular fluids. The same effect is obtained by severe sweating, which may also be employed. Attempts have recently been made by Hamburger and others to accomplish the same effect by diuretics, such as novazurol and other derivatives of theobromine. Too much time should not be lost in such attempts, which are too often without effect on the tension. *It is more rational to produce hypertonicity of the blood-plasma directly by the intravenous injection of hypertonic solutions.* This was done first by Cantonnet and Hertel, and more recent reports by Weekers, Goslich and Duke-Elder record successful results by this method. In one of Duke-Elder's cases tension was reduced from 95 to 38 mm. and in another from 58 to 20. He gives the following indications for the method: (1) In acute glaucoma, in conjunction with miotics, before operation. (2) To reduce high tension before any operation. Besides lessening the danger of vitreous loss and hemorrhage, reduction of tension allows the absorption of local anesthetics, which are ineffective in eyes with high tension. (3) In iritis glaucomatosa, before using atropine. (4) To facilitate ophthalmoscopic examination where the cornea is steamy from increased tension. Thirty-five to 50 cc. of 30 per cent sodium chloride are usually injected, or 100 to 150 cc. of 10 per cent sodium chloride, the stronger solutions producing the more rapid effect. Injections must be made slowly, and it is most important that none of the solution be injected outside the vein, which would result in deep sloughing. The author has found the use of 30 per cent sodium chloride of considerable value in a limited number of cases, including 1 case of acute glaucoma following discission in which tension fell from 60 to normal within six hours after one injection and was then kept normal by miotics. Other cases have shown no response to such treatment. As no traumatism is inflicted on the eye itself, hypertonic solutions may be tried in any case of acute

glaucoma, providing too much time is not wasted in waiting for their effect. The only contraindication is the presence of nephritis or a feeble general condition in which a marked fall of blood-pressure would be considered dangerous. Ordinarily the intake of water should be limited after the injection, which must be specifically mentioned in the orders, as intense thirst is often complained of.

A substitute for sodium chloride which is more likely to be at hand in most hospitals is *50 per cent glucose solution.* Larger amounts of this must be given, however, 100 to 150 cc., the solution being given very slowly. *The use of glucose solutions for injection has two advantages over that of sodium chloride.* The danger of producing necrosis if any fluid is injected outside the vein is absent with the glucose solution, and the effect of glucose on the blood plasma is more prolonged than that of sodium chloride, which is of short duration.

Even with glucose, however, the hypertonicity of the blood is rapidly reduced by fluid from the tissues and by loss of glucose in the urine, and this effect usually goes on until the blood is, for a time, hypotonic. Where the solution is employed to reduce intracranial pressure this effect is shown by a secondary rise of pressure. To prolong the condition of hypertonicity and avoid this secondary rise of pressure, *the use of sucrose* has been proposed. This sugar, because of the size of its molecule, does not diffuse into the tissues as glucose does, and is eliminated very slowly in the urine. Bellows and Puntenney have employed sucrose in 50 per cent solution in a group of glaucoma cases and found that its effect was of longer duration than that of glucose. A preliminary report on the use of sucrose in glaucoma was made by Dyar and Matthew, whose results were favorable. Sucrose, however, was found to damage the renal epithelium, and since it is a disaccharid it possesses the additional disadvantage that greater quantities are necessary to produce the same effect as 100 cc. of 50 per cent glucose.

Bellows, Puntenney and Cowan hence investigated the possibilities of another substance, *Sorbitol.* This is a complex alcohol with approximately the same osmotic effect as glucose. It is much less diffusible, however, practically none reaching the aqueous of experimental animals, and is much less rapidly eliminated in the urine. According to Lindbergh* it is without harmful effect on the kidneys. In 12 patients with glaucoma of various types, these investigators found that the tension could be brought to normal or nearly normal by the intravenous injection of 100 cc. of 50 per cent sorbitol. A second injection was effective in several cases in which one injection had produced an insufficient effect. The effect began within two hours but was greatest twelve to twenty-four hours after injection and continued for several days in certain cases. Since their work, the author has employed sorbitol in a number of cases of acute glaucoma and also in other types of glaucoma Its effect is usually as marked as that of glucose and has been sufficient, with the aid of miotics, to terminate acute attacks in several cases. It has been of considerable value in preparing patients for operation. In certain cases, especially of secondary glaucoma, little or no effect has been obtained, as is the case with glucose. The only disadvantage noted has been the occurrence of moderate chills, with symptoms of shock in a few patients, whereas such symptoms have rarely been seen when glucose was employed.

With glucose and salt, the effect on tension begins within two hours, and reaches a maximum within five to eight hours. With sorbitol the maximal effect is slower to appear and is more prolonged. These factors must be considered in using osmotic therapy as a preliminary to operation.

The work of Clarke on the use of *mecholyl and prostigmine,* has been discussed. (Page 51.) In acute glaucoma he used 5 per cent prostigmine and 20 per cent mecholyl by repeated *instillation, but found the most marked effect on intraocular*

* Personal communication.

tension after 25 mg. of mecholyl was injected into the retrobulbar space, preceded and followed by miotics. This was often sufficient to terminate acute attacks which had entirely resisted miotics. In our experience, his dose by retrobulbar injection is a large one, as patients have shown rather marked symptoms of shock with even smaller doses. Clarke advises

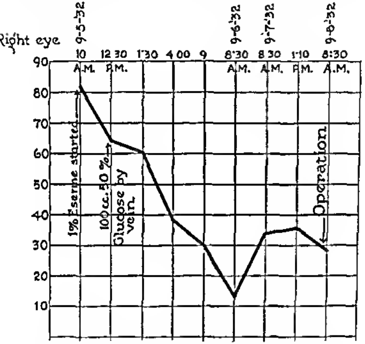

FIG 55.—Effect of intravenous injection of 50 per cent glucose in acute glaucoma.

that 1 mg. of atropine sulphate in a syringe be ready for intravenous injection when symptoms of shock occur.

A procedure which will occasionally obviate more radical surgery in acute glaucoma is **paracentesis**. Besides removing a certain amount of aqueous, it is followed by miosis and where miotics are used vigorously before and afterwards this may be maintained until the acute attack is past. Cocaine

should not be used before such a procedure, to avoid dilatation of the pupil, but holocaine or butyn. Two or 3 minims of 4 per cent novocaine should be injected subconjunctivally at the site of fixation and puncture, and a subconjunctival limbal puncture made with a narrow knife, the aqueous being allowed to escape slowly. This is practically without danger, which cannot be said of posterior sclerotomy, and may be performed with the patient in bed. This and the

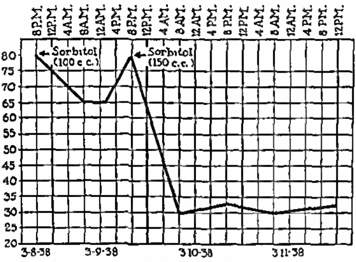

Fig 56—*Effect of intravenous injection of 50 per cent sorbitol in acute glaucoma*

use of miotics are probably our most important aids in attacking acute glaucoma, and where they fail to reduce tension there will seldom be reason for delaying operation. How much time may be spent in these procedures before resorting to surgery will depend on the height of the tension, and *where this cannot be brought below 60 it is certainly not without danger to delay more than twenty-four hours.* This is true in a case seen early in the attack, while when the attack has already been in progress for one or more days it may be inadvisable to delay operation more than a few hours.

In choosing the operative procedure one must consider whether the patient is undergoing a first attack of acute glaucoma, or has had a preëxisting chronic form of the disease. In the former case iridectomy is the classical procedure and is usually successful, while where chronic glaucoma has been present the avenues of escape for the aqueous are often permanently closed so that a filtering operation, trephining or the Lagrange procedure will be necessary.

In considering acute glaucoma Hamburger's preparation, aminglaukosan, must be mentioned, if only to emphasize its drawbacks. This is a 10 per cent solution of histamine, a powerful toxic product obtained from ergot. It has the opposite effect on the iris of glaukosan or lævoglaukosan, instillation of 1 drop being sufficient to contract an atropinized pupil to pin-point size in seven to fifteen minutes. It is advised in acute glaucoma as the most powerful miotic known, Hamburger and others having reported success in a limited number of cases by its use. A number of observers, however, have reported failures to reduce tension, and the accompanying severe chemosis of the conjunctiva, with aggravation of the preëxisting inflammation has necessitated delaying a needed operation in several cases. The author has seen such a severe reaction follow its use in one case that he is not inclined to advise it.

SECONDARY GLAUCOMA.

A necessary preliminary to any treatment in secondary glaucoma is a thorough understanding of the condition present, and, where possible, its cause. Almost any disease involving the globe may be accompanied, at some stage in its progress, by rise of tension, and this possibility must be kept constantly in mind. In iridocyclitis the occurrence of pain when the pupil is dilated with atropine or of decrease in vision not accounted for by opacities in the media should always suggest rise of tension. In such a case, when everything possible is being done for the inflammation, the mechan-

ical factor of high tension must be dealt with. Here the question of using miotics instead of atropine comes up and must be answered according to the conditions present. In an old case where the pupil is bound down to the lens and a greater or less degree of iris-bombé is present, miotics will usually be of no effect. Here a more vigorous attempt to dilate the pupil by stronger solutions of atropine will do no harm, though it will seldom be successful. *If the tension is high paracentesis with puncture of the bulging iris is indicated.* Such holes in the iris often remain open indefinitely and may control the tension permanently. If a puncture fails to control tension iridectomy is usually necessary, though it is by no means a simple procedure in such cases.

If the pupil is free, the tension being the result of so-called serous iritis, it is assumed that the highly cellular or albuminous aqueous is the cause of increased tension. In many such cases persistence in the use of atropine and the salicylates will bring the inflammation under control before serious damage is done to the eye. Larssen has reviewed a number of such cases treated with and without atropine and has concluded that most cases do better on atropine. In cases where the tension persists more than a few days on such treatment, however, miotics should be tried cautiously, 1 per cent pilocarpine or 0.2 per cent eserine being employed. As soon as the tension is under control the miotic should be stopped, and if the inflammation persists the pupil should be dilated again, preferably with homatropine. If neither miotics nor mydriatics control the tension *paracentesis is often effective* and should not be delayed too long. It has practically no dangers when properly performed, may be performed in bed or in the office, and should not he considered a major operation. According to Gradle and others, serous iritis, or iritis glaucomatosa, is an indication for the use of epinephrin. As already stated, there is evidence against this view, and further increase of tension may result from its use in certain cases, so that it must be used with great caution, if at all,

in any case of glaucoma accompanied by signs of inflammation. Ergotamine may be tried (page 53) as it is without danger to the eye, and in certain cases seems to be effective in reducing tension. In other cases it has no effect.

When the tension remains high after these procedures, including repeated paracentesis, operation, usually iridectomy may be required, even though it must be performed under unfavorable circumstances.

Since the use of the slit-lamp some cases of apparently simple glaucoma are recognized as being on an inflammatory basis, and Malling considers at least one-half to be of this nature. While this number is, in all probability, too high, and it is recognized that the presence of a few cells in the anterior chamber does not warrant the diagnosis of secondary glaucoma, there is no doubt that such cases do occur more commonly than has been believed. It is in such cases that the same search for foci of infection or other etiological factors as we are accustomed to make in iritis is indicated, and symptoms will usually be relieved only after the removal of such factors.

The *secondary glaucoma occurring in sympathetic ophthalmia* is usually due to plastic exudate which binds the iris to the lens capsule. It is especially desirable to control the inflammation without direct operative interference, since such interference may cause an access of inflammation fatal to the eye. Here, as has been stated, *ergotamine* may prove valuable, *and hypertonic solutions may be employed to keep the tension down until the crisis is past.* Atropine should usually be continued, though occasionally a cautious temporary change to miotics will be preferable. There is no rule in this matter, and the important thing is careful watch of the effect on tension of various procedures. If, in spite of these measures, tension remains high enough to endanger the nerve head operative measures should be limited to the *simplest possible procedure. Paracentesis should be tried,* with accompanying iris puncture where iris-bombé is present.

This should be preceded by the use of all possible means to prevent hemorrhage into the anterior chamber. While there is no certainty about the effect of calcium, and the various hemostatic agents, it is probably safer to employ those in which most confidence is placed for twenty-four hours before operation. A simple measure which is not used as often as it should be is that of raising the patient in bed at the first sign of oozing from the iris and keeping the head elevated for at least twenty-four hours afterward. This relieves congestion of the head and is not without effect on congestion of the ocular circulation.

Glaucoma occurs in nearly every case of intraocular tumor which is diagnosed late, and where the media are already opaque it is often impossible to diagnose such a tumor before enucleation. Many such eyes have undergone filtering operations to relieve glaucoma, resulting in increased danger of extension. The only way in which such unfortunate errors can be avoided is to follow the rule that every blind eye with increased tension, the interior of which cannot be observed, should be enucleated.

Glaucoma as a complication of diseases of the lens occurs frequently enough to require consideration. The form due to dislocation of the lens, either congenital or traumatic, is familiar enough. Where the lens remains behind the iris the effect of miotics may be sufficient to control tension and prevent further displacement of the lens forward. If the effect is insufficient operation is required, and if the lens is clear, cyclodialysis is the most logical and the safest procedure. Paracentesis is here usually contraindicated, as it allows the vitreous to come further forward. If the lens is opaque or is in the anterior chamber it must usually be extracted, a procedure requiring every precaution to avoid excessive loss of vitreous. Glaucoma from swollen cataract, usually traumatic, is usually successfully met by paracentesis, or removal of more or less of the lens substance. A type of glaucoma due to absorption of lens substance in hypermature

cataract is not as well known as it should be. It is apparently the result of toxic substances produced in the disintegration of the lens protein, is accompanied by iridocyclitis and must be considered as secondary to such inflammation. It usually requires paracentesis, repeated if necessary until subsidence of the inflammation allows the removal of the lens under favorable conditions. Glaucoma occurs after cataract extraction often enough so that it must be kept constantly in mind. This is especially true after extracapsular extraction in which cortex has been left in the eye, while it is rare after uncomplicated intracapsular extraction. It also occurs after discission in an appreciable number of cases. When diagnosed early, the vigorous use of miotics may bring it under control. In other cases the use of epinephrine packs or instillations, together with miotics, is effective. In a number of cases these measures are unsuccessful in controlling tension and operation is required. The filtering operations and iridectomy are very apt to be ineffective under these conditions, and *cyclodialysis is coming to be recognized as the operation of choice.*

Glaucoma following thrombosis of the central vein is usually unaffected by treatment when it has once developed and often requires enucleation. There is some evidence that it may be prevented by the prophylactic use of miotics immediately after the vascular lesion has occurred and for long periods following it. The possible value of roentgen therapy and heparin in preventing this complication is discussed on page 324.

Recent observations by Poos indicate that rise of tension during diabetes may be the result of insulin. This is an osmotic phenomenon dependent on sudden lowering of the blood sugar with consequent dilution of the blood plasma. It should be watched for, and may be an indication for stopping insulin for a time. Besides this type, inflammatory glaucoma is a not infrequent occurrence in diabetes, and requires

the ordinary local therapy in addition to measures directed to the control of diabetes. It is usually the result of some intercurrent infection and may have a serious prognosis.

ABSOLUTE GLAUCOMA.

The treatment of absolute glaucoma is necessarily limited to the control of pain. *The only certain way to afford permanent relief is removal of the eye.* Treatment with miotics is usually ineffective, and the other methods described here give *only temporary relief, if any. Operation to reduce* tension is sometimes successful, but more often the tension and pain return and enucleation must then be performed. *The use of retrobular injections of alcohol* proposed by Gruter has apparently given permanent relief in some cases, and may always be tried, as it may in the case of any blind painful eye. One cubic centimeter of 2 per cent novocaine is first injected with a curved needle, 4 cm. long, deep into the orbit, the needle being inserted between the external and inferior recti. After waiting five minutes 2 cc. of 80 per cent alcohol are injected in the same location. Both injections may also be divided between two or more quadrants of the orbit, but in this case the risk of striking a large vessel is greater. More or less complete oculomotor paralysis and anesthesia of the globe results, but if the muscles are avoided the paralysis clears up and the anesthesia becomes only partial, while the pain is relieved permanently in favorable cases. Out of 56 cases injected by Gruter a repetition of the injection was necessary in only 5 cases. Keratitis developed in 5 cases, but was severe in only 2. The other cases showed almost complete relief from pain, some having been followed for five years. Others have reported success by this method, although in some cases the oculomotor paralysis has remained permanently, while in a few others hemorrhage or severe reaction has necessitated enucleation. *In spite of a few*

CHAPTER XII

DISEASES OF THE RETINA.

VASCULAR LESIONS.

Closure of the Central Retinal Artery.—Closure of the central retinal artery *comes on with dramatic suddenness and anything which is done for it must be done with almost equal rapidity.* Loss of the retinal blood supply results in permanent degenerative changes in the retina after a very short time, varying from a few hours in complete obstruction to one or more days, where it must be assumed that obstruction was not complete. Wegner found that permanent changes in the retina were produced by complete obstruction lasting only forty-five minutes. A clinical differentiation between embolism and thrombosis is usually impossible except in cases with mitral stenosis or endocarditis, but we know from Scheerer's work that thrombosis is much the more common. Our efforts are reduced *to producing sudden peripheral vasodilatation* in the hope that the obstructed vessel will dilate enough to allow a renewal of the circulation or to allow the embolus to pass to a smaller vessel. The standard method of producing such vasodilatation is by the immediate inhalation of *amyl nitrite.* Haessler found, however, by photographic methods that no change great enough to be detected was effected in his cases by this drug.

Recent work by Lambert with a device by which the vessels could be photographed under high magnification casts doubt on the possibility of favorably affecting the retinal circulation by vasodilators. He found that in the rabbit administration of vasodilators sufficient to lower the blood-pressure was accompanied by an actual decrease in the size of the retinal arterioles, while when the blood-pressure was elevated by epinephrin, an increase in the size of these vessels resulted. Lambert explains these results by the fact that

the retinal arterioles possess no true muscularis, and hence respond passively to changes in the general circulation. While it is difficult to reconcile this with reported clinical results and with the occurrence of retinal arterial spasm under certain conditions, this work challenges further investigation and may materially modify our views on therapy.* Until the matter is decided, use of the vasodilators will probably be continued in certain conditions.

A more effective method, if the case is seen early, is to reduce the intraocular tension by paracentesis. The aqueous is allowed to escape completely, and an attempt is made to maintain the consequent vasodilatation by continuing the nitrites. Some remarkable recoveries of vision have been reported after this procedure, and there is no doubt that any patient seen within twelve to twenty-four hours after closure of the central artery should be treated in this way, and without the loss of an hour. While preparing for paracentesis an inhalation of amyl nitrite should be given. Vigorous massage of the cornea through the closed lids will also reduce the tension, but not to the same extent as paracentesis, which should always be performed first. After the first inhalation of amyl nitrite a more prolonged vasodilatation is secured by giving nitroglycerin, $\frac{1}{100}$ grain, subcutaneously, or sodium nitrite, 1 grain, by mouth, three times a day, this being continued for several days. If the case is seen on the second or third day similar treatment may be tried, but without the same hope of recovery. Pilocarpine sweats may also be tried. In cases seen later than this treatment will usually be without effect, and all that can be done is to advise care of the general condition to avoid a similar occurrence in the other eye. Where only one branch of the central artery is affected treatment will be the same.

It is becoming recognized that a number of cases of closure of the central artery are due to *spasm of the vessel*, a condition analogous to intermittent claudication or thrombo-

* These findings were confirmed by Vantenney.

angiitis obliterans of the extremities. Where the closure occurs in a young adult without arteriosclerosis, with a history of numerous previous attacks of temporary monocular blindness, it will be considered as most probably of this type. Even when arteriosclerosis is present, the additional *factor of spasm is often important* in maintaining complete occlusion of a vessel. Inhalation of amyl nitrite is usually advised in an attempt to produce relaxation of vascular spasm. Duggan believes, however, that a more powerful *effect is produced by intravenous injection of 1 cc. of 10 per cent sodium nitrite.*

Acetylcholin has been advocated by a number of ophthalmologists, especially in France, and the references to St. Martin and Schiff-Wertheimer are only a small part of those reports available which refer to remarkable recoveries of vision following its use. One-tenth to 0.2 gram is injected intramuscularly, daily injections being continued for eight to fifteen days. The very brief action of acetylcholin resulting from its destruction by cholinesterase has been mentioned (page 51). In view of this, such results, some of which occurred several weeks after the occlusion, are difficult to explain as the result of treatment. The author has tried acetylcholin in a number of cases, but without observing notable effects. Puntenney observed some dilatation of the retinal vessels following the *retrobulbar injection of mecholyl.* He employed from 10 to 15 mg. of the drug, with the same precautions as those observed by Clarke to combat shock. The action of this drug is more prolonged than that of acetylcholin and its use by this method would seem to be well worth a trial in cases seen within the first two days. In those seen later, with complete occlusion, all procedures are likely to be ineffective.

Thrombosis of the Central Retinal Vein.—When complete closure of the vein has occurred treatment has usually proven ineffective in restoring any useful vision. The use of roentgen therapy has been described, with the favorable results of

The use of heparin is somewhat costly and requires hospitalization with adequate personnel for control of the clotting-time. In a condition which presents such a poor prognosis, however, when treated by other means, the results so far reported seem to justify a thorough trial of heparin. It should be begun as early after the onset of symptoms as possible and adequate dosage should be continued for five to eight days. The use of small doses given for shorter periods is not likely to give any information as to the value of the method.

The prevention and treatment of glaucoma following central vein thrombosis has been discussed on page 318.

Another consideration in such cases is the prevention of a similar occurrence in the other eye. This indicates a careful general examination with employment of whatever measures are indicated to improve or preserve the circulatory apparatus. In the somewhat rare cases of young adults affected by the condition, a search for foci of infection may be of value and blood tests for syphilis are indicated in any case.

Diabetic Retinopathy.—The lesions of the central retina which occur in diabetes apparently result from changes in the capillary bed resulting in small thromboses and areas of cellular necrosis. Such patients show increased capillary fragility when the skin is subjected to pressure and in some cases dietary deficiencies are present. These facts stimulated Friedenwald to employ cevitamic acid and vitamin B complex in cases of diabetic retinopathy, with results which at first seemed encouraging but which he later felt were not conclusive. In the discussion on page 84 reasons were given for assuring an ample supply of the essential vitamins in this condition. Now that the supposed antifragility factor, citrin or vitamin P, is available in limited amounts, a trial of its use in diabetic retinopathy would seem indicated. The existence of retinopathy in a diabetic, as well as the other vascular lesions such as proliferative retinitis and recurrent vitreous hemorrhages, is of course an urgent indication for most careful diabetic control.

Arteriosclerotic and Hypertensive Retinopathy are, in general, little affected by any form of treatment. General measures for control of blood-pressure, when effective, will prevent to some extent the progress of retinal lesions, and certain methods recently available, including the use of the sulfocyanates and sympathectomy, have resulted in considerable improvement of vision as well as prolongation of life in patients formerly considered hopeless.

Central Angiospastic Retinopathy.—Under this name a group of cases has been described which seems to depend on spastic closure of the fine end-vessels supplying the macula. The condition affects young adults, especially males, who smoke, and nearly all cases showed a pathological degree of peripheral vascular spasm. Spontaneous recovery often occurs, but recurrences are common and may result in considerable loss of central vision. Patients were kept free from recurrence and their lesions seemed to clear more rapidly when they were placed on so-called antispasmodic treatment. This includes complete abstinence from tobacco, small doses of barbital and, during the active stage, repeated small intravenous injections of typhoid vaccine or insulin-free pancreatic extract for its effect in producing peripheral vasodilatation. Adequate rest and a diet containing adequate vitamins are essential parts of treatment. It is important to distinguish such cases from toxic amblyopia and retrobulbar neuritis, since in some cases the macular lesions are very delicate. More severe cases, in the author's opinion, are sometimes wrongly called central retinitis when in reality a functional disturbance of the vessels and not an infection is at fault. Examination of the peripheral vascular system by an internist specially trained in this field will afford information of value and indications for treatment in certain doubtful cases.

Periphlebitis Retinæ.—This condition, often associated with recurrent hemorrhages into the vitreous, is undoubtedly in

many cases due to tuberculosis. Where sensitivity to tuberculin is high and chest plates offer suggestive evidence, the retinal changes may usually be considered to be tuberculous. Treatment in such cases consists chiefly in complete rest for long periods and an adequate diet. Sunlight or general phototherapy is probably of value and a change in climate may be advisable. The use of tuberculin involves special danger of focal reaction in this condition and is seldom advised. If employed at all, the initial dosage should be exceedingly small, about one-hundredth of that employed in chronic iridocyclitis, and should be increased very slowly.

Marchesani has described a group of cases with periphlebitis which showed evidence of Buerger's disease. While the number of such cases is probably small, the possibility is sufficient so that examination of the peripheral vascular system should be advised in patients who show no signs of tuberculosis. *If signs of peripheral vascular spasm are* found, the antispasmodic treatment previously described may prove of value.

RETINAL DETACHMENT.

Since the recent work of Gonin, Lindner, Guist, Weve and others, it may be said that *the treatment of this condition is nearly always surgical.* If a retinal tear is found in a case not more than two months old one will attempt to close it by the cautery, according to Gonin, or as is now more frequently done, by diathermy coagulation. If no tear is found one may employ the use of the electrocoagulating current to the sclera, as advised by Larssen. The use of hypertonic sodium chloride injections and pilocarpine sweats once almost universally employed, seems to have no place in the modern treatment of retinal detachment. It must be remembered that the retinal detachment occurring in nephritis and the toxemias of pregnancy tends to heal when pregnancy

is terminated and does not require surgical intervention. In this period of enthusiasm over the operative treatment of detachment extreme care must be exercised in diagnosis to avoid operating upon cases of detachment due to intraocular tumors.

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CHAPTER XIII.

DISEASES OF THE OPTIC NERVES AND CENTRAL VISUAL PATHWAYS.

OPTIC NEURITIS AND RETROBULBAR NEURITIS.

Typical optic neuritis with visible changes in the disc and *retrobulbar neuritis* without any visible changes *are both due to the same causes, and their treatment is essentially the same* It happens that syphilis is more frequently responsible for frank optic neuritis, while multiple sclerosis more often causes the retrobulbar type. Various toxic substances have predilections for one or the other portions of the optic nerve. Thus lead is apt to produce visible changes in the nervehead, while carbon monoxide and thallium, in the cases so far reported, have affected the retrobulbar portions. Methyl alcohol has produced both types of neuritis.

The first duty of the ophthalmologist is the prompt employment of every aid in establishing an etiological diagnosis This should include serological tests for syphilis and undulant fever, neurological examination and a careful history of possible exposure to various toxins. Those which are known to have caused optic neuritis of one or both types include methyl and ethyl alcohol, thallium, lead, carhon tetrachloride, carbon disulphide, benzol, carbon monoxide, trichlorethylene, arsenic, especially tryparsamide, sulfanilamide and a number of others. Various drugs such as quinine, santonin, male fern and even digitalis are responsible for occasional cases. When inquiries as to the above causes are negative, spinal puncture, roentgenograms of the paranasal sinuses and a search for frank foci of infection are indicated. Infected tonsils and teeth are only rarely responsible for optic neuritis but their elimination as possible causes is occasionally advisable. Infected sinuses are more frequently responsible, although

emphasis on their importance has diminished in recent years. Many suspicious sinuses have been opened, followed by recovery of vision, but in some of these cases later attacks have occurred, accompanied by unmistakable signs of multiple sclerosis. When definite infection of the sphenoids and ethmoids can be demonstrated, however, prompt and adequate treatment of this condition is indicated. It must be remembered that *multiple sclerosis is responsible for at least 60 per cent of the cases of retrobulbar neuritis* and that involvement of one or both optic nerves often precedes by years the appearance of any other clinical signs of the disease. Recovery of vision following any therapeutic procedure is no proof that multiple sclerosis was not the cause, since spontaneous recovery is common, nor does such recovery offer any guarantee against recurrence.

When the tests for syphilis are positive, in early cases rigorous antiluetic treatment usually brings about prompt recovery. The author has not seen harmful reactions from the use of neoarsphenamine in such cases, in spite of the common teaching to the contrary. Such treatment is accompanied by mercury or bismuth and followed by potassium iodide. Cases due to the various toxic substances improve on removal of the cause if irreparable damage to the nerve has not already occurred. In the case of certain substances, such as methyl alcohol, *spinal drainage*, repeated one or more times, may be of value. Damage from tryparsamide is best treated by intravenous injections of *sodium thiosulphate*, which aids the elimination of arsenic in the form of a less harmful compound, 10 cc. of 10 per cent solution is given daily for several days.

Certain non-specific forms of treatment are of apparent value in many cases of optic neuritis and *may well be begun as soon as the patient is seen.* Some of these, such as non-specific protein therapy and use of vasodilators, depend on an increased supply of blood and antibodies to the nerve, while the use of thiamine chloride is justified by a possible deficiency or by increased need for this substance by damaged nerve

tissue. Duggan argues for the use of *active vasodilatation* in all cases, and the results in his series were excellent, whether or not evidence of multiple sclerosis was present. He employed 1 cc. of 10 per cent sodium nitrite by vein daily for an average of eight days, the number of injections depending upon the response to treatment. Eighty-six per cent of his 29 cases of retrobulbar neuritis recovered vision of 20/30 to 20/15. Most were not followed long after the first attack although treatment of recurrences in several cases was followed by a similar response. Most ophthalmologists have depended more upon the use of *foreign protein, especially intravenous typhoid vaccine* and results have been, on the whole, much more favorable than those in the control series of untreated cases reported by Duggan In the author's series of 18 cases, for example, all but 3, or 83 per cent, recovered vision of 20/40 or better following the first attack while in all but 1 of these vision was 20/25 to 20/15. These cases were given typhoid vaccine, with, in recent cases, large doses of thiamine chloride by vein and later, by mouth. The dosage of foreign protein is discussed on page 139 and that of thiamine chloride on page 80. There is no objection to the combined use of either vasodilators or foreign protein with thiamine chloride and one of these two combinations should probably be advised in all cases except those due to syphilis. In cases due to various toxic substances, similar treatment is not harmful and may be beneficial.

In spite of a favorable response to such treatment, cases should be observed over long periods for signs of multiple sclerosis or other systemic disease. In the prevention and treatment of multiple sclerosis rest is thought to be important and the resumption of strenuous physical effort soon after an attack of retrobulbar neuritis would seem ill-advised. In addition the continued supply of thiamine chloride or vitamin B complex in adequate amounts may not be without effect on that disease. Regulation of the diet with this end

in mind may suffice but the use of the concentrates for a considerable time is often advisable.

When, in what has been called retrobulbar neuritis, treatment does not result in appreciable recovery of vision after four to six weeks, one must reconsider the case most carefully. *Possible intracranial causes of pressure on the nerves must be especially considered.* Tumors of the frontal lobe and meningiomas of the olfactory groove are known to exert direct pressure on one optic nerve before signs of increased intracranial pressure become manifest, and reëxamination by neurologist and roentgenologist with these possibilities in mind may produce evidence pointing to one of these conditions. Arachnoiditis nearly always involves both nerves and hence the field of vision of the apparently healthy eye must always be taken. Field changes which suggest pressure on both nerves or on the chiasm must arouse suspicion of this condition and also of pituitary tumor. Such suspicion may receive enough foundation to justify exploration of the chiasm by a neurosurgeon. Every ophthalmologist of experience can remember personal cases in which such exploration was the means of saving patients from death or blindness.

TOXIC AMBLYOPIA.

As has been stated (page 81) our ideas concerning toxic amblyopia have undergone radical revision since the work of Carroll, Johnson and others on thiamine chloride. The term is used to describe the chronic form of optic nerve degeneration, usually resulting from abuse of alcohol alone or in combination with tobacco, and resulting in bilateral slowly progressive loss of central vision with centrocecal scotomata. It is to be distinguished from the acute loss of vision which may occur in alcoholics and which has been considered under the group of acute neuritides.

The common existence of a dietary insufficiency in alcoholics has been discussed, and their need for an increased

supply of thiamine chloride. The same deficiency may exist in diabetics who are known to be especially liable to develop toxic amblyopia when employing alcohol and tobacco in only moderate amounts. The occurrence of amblyopia in smokers who do not drink is not common, but does occur, and is possibly due to the prolonged effect of peripheral angiospasm resulting from tobacco. Carroll feels that the use of thiamine chloride is of value in such cases of amblyopia, as well as in those due to alcohol. He showed that recovery from toxic amblyopia occurred following the use of adequate amounts of thiamine, even when the previous consumption of alcohol and tobacco was continued, as was the case in other forms of alcoholic neuritis. Hence, it must now be admitted that *toxic amblyopia behaves like a deficiency disease and that supplying the deficiency must be the essential part of our therapy.*

Initial dosage should be large, 16,000 units a day by vein for six to ten days being usually advised. Vision improves on such therapy within a week in early cases, when 7000 units or 20 mg. a day by mouth may be sufficient Additional vitamin B complex is often employed, for reasons which have been stated. Alcohol and tobacco are usually prohibited or greatly restricted during recovery and if possible this restriction should be continued, although total abstinence from tobacco, a requirement which is refused by many patients, is probably unnecessary. Advice as to the diet should be given and may be followed if its importance is emphasized In cases of long standing, recovery may be quite slow but Carroll reports cases in which improvement occurred after months or even a year of treatment. Duggan has seen good effects from the use of intravenous sodium nitrite in this condition, as well as in retrobulbar neuritis. There may be similar reasons to explain this and vasodilators may be employed with thiamine if improvement in vision is delayed. In such a chronic condition the use of sodium nitrite or nitroglycerine by mouth would seem preferable to intravenous therapy.

In addition to the typical condition occurring in alcoholics, the author has seen a *few cases in middle aged abstainers from alcohol-tobacco* with reduction of vision from 20/15 to 20/30 or 20/40 and without typical scotomata, in which vision improved to normal on large doses of thiamine. Evidence of liver damage was present in 1 case and dietary deficiency in another. The fact that a similar picture may develop in *pernicious anemia* should also be remembered and is an indication for careful blood examination and gastric analysis in puzzling cases. In such cases the use of liver extract has caused improvement in vision or prevented further loss.

OPTIC ATROPHY.

This condition must be considered according to its causes. Atrophy occurring in multiple sclerosis is probably always preceded by optic neuritis or retrobulbar neuritis. While treatment in the acute stages may be of some value, as discussed above, nothing can be done when the stage of atrophy has set in.

Optic atrophy may be the result of arteriosclerosis affecting the nutritive vessels of the nerve. The diagnosis is made by exclusion and by the signs of general arteriosclerosis, and treatment must be limited to general measures. If the onset is sudden, so that spasm of these vessels is suspected, the same type of therapy with drugs causing vasodilatation as has been described in the treatment of disease of the retinal arteries may be tried, but in most cases this remains ineffective.

The *commonest cause of optic atrophy is, of course, syphilis of the central nervous system.* While it is common in tabes and paresis, it occurs in many cases as almost the only sign of syphilis, or as the only sign remaining after a course of treatment. While the blood Wassermann is often negative in these cases, examination of the spinal fluid will nearly always show a positive complement-fixation test and increased

globulin and cell count. In such cases many ophthalmologists believe all treatment to be practically useless. Many avoid the arsenicals in such cases, fearing damage to the nerve itself by these drugs, and Behr advises only the most conservative treatment, chiefly with mercury and the iodides. These views depend upon the old belief that luetic optic atrophy is a purely degenerative process and on the observation of many cases which have progressed to blindness during general antiluetic treatment. There is a large body of evidence, however, most of which was summarized in articles by the author, that this view is not correct, and that an inflammatory process is present at some point along the course of the nerves, as is the case in other forms of syphilis of the central nervous system. If spirochetes are not present in the nerve itself they have been found in its sheaths and in the meninges near the chiasm by Igersheimer. Such a view of optic atrophy as the result of active luetic neuritis or perineuritis is in line with modern views on syphilis of the central system. If it is correct it offers the possibility as long as useful vision remains that the active process may be brought to a standstill and this vision preserved. It offers no hope, of course, that the function of already degenerated nerve fibers will be restored.

As in syphilis of the central nervous system, *general treatment in luetic optic atrophy has proven of little value.* Various methods have been employed with the object of bringing antispecific medication in closer contact with the diseased part than was possible by the oral or intravenous routes Spinal drainage combined with intravenous injection of arsphenamine was advised by Dercum, and was tried by the author, but without effect, and the method has not come into general use in other forms of central nervous system syphilis. Arsphenamine or arsphenaminized serum given intraspinally by the Swift-Ellis method has been used by a number of ophthalmologists, and Zimmerman, Fordyce, and Bruner have reported favorably upon this method in cases of optic

men is saved for examination and 4 to 5 drops of 1 to 200 mercuric chloride solution are added to the remaining fluid and allowed to flow back slowly by gravity. The procedure was followed after twelve to twenty-four hours by an intravenous injection of neoarsphenamine. Mercury was administered until the next injection which was given after six weeks. Three or four injections were given in most cases.

In the early cases reported, reactions, including headache, vomiting and hyperpyrexia were never alarming. Following injection by a competent neurosurgeon in a later case, however, a fatality occurred and other fatalities were reported by Suker and Jacobson. Hence, in spite of the encouraging results in other cases, *it must be concluded that the dangers of the method are out of proportion to its advantages.*

The use of *air injections* into the cisterna magna, as employed by Fazakas and by Lowenstein, probably depends, like the preceding and other methods of subdural injection, upon the production of an aseptic meningeal irritation with increased permeability of the meninges. Although no fatalities are known to have followed air injection in this condition, the method would seem subject to dangers similar to those of the method just described.

Another mode of attack in this disease is *the artificial production of hyperthermia by the use of malarial inoculation as practised in general paralysis.*

Reports by Fischer-Ascher, Heinsius, Gasteiger, Clark and others include a few cases in which vision and fields improved slightly after treatment, while in a large number no progress in the atrophy occurred during a fairly long period of observation. Results at least as good were obtained by Culler and Simpson with *fever induced by the air-conditioned cabinet.* Sixteen patients were observed for an average period of twenty months and in only 3 was a slight decrease in the fields noted. The same degree of fever were produced as in treating interstitial keratitis, 105° F. for five hours repeated in ten weekly treatments. The advantages of this

method for producing fever over the use of malarial inoculations are obvious.

The *production of fever by injections of sulphur* has been tried in luetic optic atrophy by Winkler, Busacca and others. A 1 per cent suspension in olive oil is injected intra-muscularly, $\frac{1}{2}$ to 2 mg. of sulphur being usually sufficient to produce temperatures of 38.5 to 39° C. The reactions were by no means uniform, however, and the use of the cabinet would seem preferable where it is available.

Moore and Woods have summarized the reported results of fever therapy in 343 patients. Of those treated by malaria 54.5 per cent were apparently arrested, while in a much smaller series given fever by mechanical means the percentage of arrest or improvement was 70 per cent.

There seems to be no doubt that both the methods of intraspinal injection and fever therapy have definite advantages in this condition over systemic use of antiluetic therapy alone and that patients with luetic optic atrophy should be given the advantage of one of these methods as soon as the diagnosis is made. The prognosis in early cases when treated by either method, while doubtful, is by no means so hopeless as in former years. In cases with no useful vision remaining, no results can be expected from treatment.

Neoarsphenamine following injections or fever treatments is apparently an important aid, and its reputation for causing damage to the nerve is probably the result of damage caused by the disease itself. Other arsenicals, such as atoxyl and tryparsamide we do know to be dangerous, and these pentavalent arsenicals are absolutely contraindicated in optic atrophy. A case of general paralysis or tabes should not be given tryparsamide until the integrity of the optic nerves is proved by examination of the vision and visual fields.

Recent reports by Vail and Hausmann have proved that optic atrophy in a certain group of patients with syphilis is *not due to disease of the nerves themselves but to the presence of arachnoiditis* with the formation of bands which compress the

nerves or optic chiasm. Such a condition may be suspected when the visual fields show hemianopic or symmetrical horizontal defects suggestive of pressure on the chiasm. It must also be considered in any case with visual loss which progresses in spite of treatment. The usual diagnostic methods, including air studies, are not of much value. *When a diagnosis can be made, exposure of the chiasm by a neurosurgeon is indicated.* Freeing of the bands has resulted in arrest of the condition in a number of cases, and in marked improvement of vision in others. The author has seen 2 cases in which marked improvement followed such surgical treatment. A few operative fatalities have occurred, but the risk seems justified when diagnostic evidence points definitely to the condition.

Arachnoiditis of non-specific origin accounts for a certain percentage of cases of optic atrophy. It may be suspected when field defects show involvement of both nerves in the region of the chiasm, and when evidences of pituitary tumor are absent. In some cases it will be impossible to exclude pituitary or suprasellar tumor without exploration of the chiasm which is indicated in both conditions. Optic atrophy resulting from various toxic substances and from multiple sclerosis is the result of retrobulbar neuritis and the treatment of this condition, in the stage before atrophy occurs, has been discussed.

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CHAPTER XIV.

DISEASES OF THE LACRIMAL APPARATUS.

STENOSIS OF THE NASOLACRIMAL DUCT.

While this condition is usually associated sooner or later with dacryocystitis, it is sometimes seen before any such infection has occurred and in some cases the condition of simple stenosis persists indefinitely. *Congenital stenosis* is much commoner than is generally believed, and since its symptoms are limited to an excess of tears in the eye with slight redness of the conjunctiva, it is often mistaken for conjunctivitis and treated as such. No form of medication is of any value in this condition, which *is usually simply relieved by passing a large probe, No. 10 Bowman's or the Weber probe, through the nasolacrimal duct* and puncturing the thin membrane between this duct and the inferior meatus. This must be done under general anesthesia in babies and young children, and in order to pass a large enough probe, the upper tear-point must be dilated and the upper canaliculus (never the lower) slit with a fine canaliculus knife. There need be no fear of passing such an apparently large probe as No. 10 Bowman's even in small infants. There is less danger of making a false passage with such a probe than with a smaller one, the only necessary precaution being that the point of the probe is in the opening of the duct and that the direction is correct. (Fig. 57.) Great pressure is never necessary in simple congenital stenosis if these precautions are followed. After leaving the probe in place one minute it is removed, and normal saline is injected through the dilated canaliculus into the nose, to be sure that an opening has been made. Usually one such probing is all that is necessary, as the opening in the membrane is kept open by the flow of tears through the duct. In occasional cases it may be

necessary to repeat it one or more times. It is important that proper diagnosis and treatment be instituted as early as possible in these cases, as when the duct remains closed infection is likely to occur at any time, and then the condition is as unsatisfactory to treat as chronic dacryocystitis in the adult.

Simple stenosis in the adult may be the result of untreated congenital stenosis or of inflammatory changes of nasal origin in the walls of the duct. It is usually accompanied by hypertrophy of the bone or the formation of new connective tissue scars which make its treatment much more complicated than the simple congenital form in children. In a few cases probing with small probes through the dilated (but not slit) lower canaliculus may be effective. Usually the effort is only temporary and the procedure must be repeated so often that the patient becomes discouraged. *Probing with large probes, as advocated by Ziegler, is much more effective*, and by its means a number of cases may be permanently relieved. This requires slitting the upper canaliculus along its whole length, so that the probe may be inserted directly into the common canaliculus and passed almost straight down to the opening of the duct. This incision need be done only once, since such a cut remains open for any number of future probings. It has no effect upon the capillary drainage of tears through the lower canaliculus, which should never be incised for the purpose of probing.

FIG 57.—Proper position of probe in nasolacrimal duct.

Incision of the upper canaliculus and the first probing is

best done after careful infiltration with 4 per cent novocaine. The tissues all along the canaliculus and as close as possible to it are infiltrated and then the region of the sac, extending as far down over the first part of the duct as possible. After the canaliculus is incised a drop of 10 per cent cocaine is injected directly into the sac, and this is repeated twice. Then a No. 6 Bowman's probe or small Weber probe is passed into the duct. This may require considerable force *and unless it can be felt that* progress is being *made* with the probe it must be decided that the direction is not correct, or that a firm bony obstruction will make probing impossible. Once the No. 6 probe has been passed a drop of 10 per cent cocaine can be injected, and if this is repeated a No. 10 or No. 12 probe can usually be passed with very little pain. This should be left in place five or ten minutes and the duct irrigated when it is withdrawn.

It is important to repeat such a probing, if possible, the next day or after two days, as at this time the effect of the first probing is still evident, and fluid can be injected through the duct. The opening of the slit upper canaliculus should be touched with 10 per cent cocaine and then 1 or 2 drops are injected through the duct. If this is repeated after two minutes the probing can usually be carried out with practically *no pain.* The interval can then usually be lengthened to two or three days, and after several such treatments at *increasing intervals* drainage *of the* tears *may be quite* efficient and remain so for long periods. Usually such patients require an occasional probing for a long time, but are fairly free from the symptoms of obstruction in the interim. If a member of the patient's family can be taught to wash through the duct with a 0.2 per cent zinc chloride solution every day, which is relatively easy when the upper canaliculus is slit, this is of great value in keeping the duct open. *In spite of this treatment there are a number of cases whose stenosis recurs after every probing, and in these cases*

we are obliged to advise a dacryocystorhinostomy or to abandon the treatment without this.

Probing the nasolacrimal duct becomes a painful and impossible procedure unless every care is taken to obtain good local anesthesia. Before dilating the punctum for diagnostic injection of fluid it should be touched two or three times at two-minute intervals with 10 per cent cocaine on a small applicator. Having dilated it with a conical dilator,

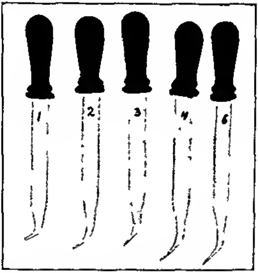

FIG 58.—Droppers made in various shapes for irrigation of the lacrimal passages.

a drop of 10 per cent cocaine is injected through the canaliculus as far as it will go. This is repeated twice, and in this way the lining of the canaliculus and part of the sac is usually fairly well anesthetized. Sometimes the shrinking effect of the cocaine will then allow the solution to be injected into the nose. For such injections an ordinary Luer syringe with special gold lacrimal tips is employed by most ophthalmologists. These tips are satisfactory for injecting

through the tear-points, but are not large enough to fill the opening when the upper canaliculus has been slit, and hence very little pressure can be obtained. Glass droppers drawn out to points of various sizes, make it possible to inject with considerable force through openings of any size, and offer considerable advantages over the ordinary syringe. (Fig. 58.) The rubber tops must be tied on securely with silk thread, and changed when they become old. Such droppers should be kept in some container to prevent the delicate glass tips from being broken. Ordinary care will prevent these tips from being broken off in the canaliculus. The larger tipped droppers may be given to the patient for irrigations at home.

ACUTE DACRYOCYSTITIS.

When a case of this condition is first seen it is usually at a stage when immediate incision is required. The pain of this incision can be much lessened by careful infiltration with 4 per cent novocaine and adrenalin if the injection is begun away from the swollen and inflamed area and carried out very slowly. In some cases, light gas anesthesia will be preferred. *The incision must extend to the bone of the lacrimal fossa* and should be 1 cm. long to allow free drainage. Free pus can nearly always be obtained, and if it is not it is usually because the incision is not deep enough. The wound should be kept open for twenty-four to forty-eight hours by a wick of iodoform gauze extending into the sac, or by a U-shaped drain of silver wire, which is easier to remove. A moist dressing should be applied and changed every twenty-four hours, when the drain is removed and replaced. After forty-eight hours the swelling has usually subsided to a great extent, and the wound may be allowed to close. It is best, however, to test the permeability of the duct, and if fluid cannot be injected into the nose, to probe the duct with a No. 10 Bowman's probe through the incision. The inside of the sac and opening of the duct can be anesthetized by

leaving a small applicator soaked in 10 or 20 per cent cocaine in the sac for five minutes. Special care must be taken not to make a false passage in the presence of an acute infection, and one must not persist in the attempt to probe or inject where this is not possible with moderate pressure. Such a probing where successful may permit the drainage of tears without further treatment. More often the acute attack is only an incident in chronic dacryocystitis, and in these cases the usual treatment for that condition must be employed after the acute inflammation has subsided.

When a case is seen in the first stage of inflammation, with very little swelling and no fluctuation, it may be possible to bring about resolution of the acute attack by packs of a saturated solution of Epsom salts, or by hot packs.

A number of cases have been reported in which adequate dosage of *sulfanilamide* by mouth has caused rapid resolution of acute dacryocystitis without incision. In early cases an attempt at securing this result may well be made.

The author has seen 2 recent cases in which a procedure without the objection of a skin incision has proved very effective. They were early cases with only moderate swelling and no objective signs of localized abscess, but with severe pain and lacrimation. After injecting 4 per cent novocaine very slowly along the upper canaliculus, this was slit and a Weber probe was passed into the lacrimal sac. Its withdrawal was followed by a flow of pus from the sac. The pain was relieved at once and by the next day fluid could be injected freely through the duct. Lacrimation was relieved and has not recurred.

CHRONIC DACRYOCYSTITIS.

This is *the usual result of nasolacrimal duct stenosis*. The choice of treatment depends on several factors. If the condition is of many years' standing, and the lacrimal sac is much enlarged and filled with mucoid or mucopurulent material, it may be impossible to obtain permanent drainage even if

the duct can be probed without difficulty. Bony hypertrophy of the duct walls may make probing impossible and this is usually the case where the obstruction is due to injury to the bones of the face or to congenital lues. If the patient is of advanced years, and treatment of the condition is considered as a preliminary to cataract operation, or is necessitated by the presence of a serpent ulcer, any prolonged course of treatment is contraindicated. *Under these conditions it is best to resort at once to an operation for radical cure of the condition.*

In a young person one will feel inclined to try some procedure which will preserve the lacrimal drainage, either a modified West operation through the nose or the external operations of Mosher-Toti or Dupuy-Dutemps. One who is familiar with the technique of any of these operations can obtain a good proportion of permanent cures by their means, though the obstruction recurs in a certain number operated upon by any method.

Excision of the sac or destruction of its lining by trichloracetic acid should in nearly every case relieve the mucopurulent discharge aod remove entirely the focus of microörganisms which renders any intraocular operation or trauma to the cornea exceedingly dangerous to the integrity of the globe. One of these procedures is absolutely required before cataract operation or in the presence of serpent ulcer.

Excision of the sac must be considered a hospital operation, chiefly because of the troublesome bleeding sometimes encountered. In destruction of the sac by trichloracetic acid, according to H. Gifford's method, this difficulty is seldom encountered. Hence it may be performed in a well-equipped office, and its technique will be briefly described here. (Fig. 59.)

The patient is seated, so that the acid may not run out of the canaliculi into the conjunctival sac. The skin is protected by thick zinc oxide ointment. The region of the sac is thoroughly infiltrated with 4 per cent novocaine. The

incision is the same as for an excision of the sac, but may be considerably shorter, and must go into the sac, as shown by a probe passed through the lower canaliculus. All bleeding is stopped, and the interior of the sac dried with applicators. The lips of the incision in the sac are held apart by a pair of iris forceps whose tips are bent backward to form a self-retaining speculum. The ordinary lacrimal sac speculum may serve as well, but its teeth are apt to be too short.

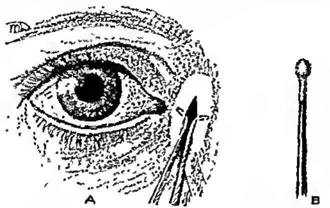

Fig. 59.—Destruction of the lacrimal sac with trichloracetic acid. *A*, incision, skin protected by zinc oxide; *B*, applicator for use of trichloracetic acid.

Immediately after drying the sac 2 drops of pure liquefied trichloracetic acid are placed in it and rubbed thoroughly into all parts of the wall by an iron applicator with a small ball of cotton wrapped closely near its end, so that the cotton may not touch the skin. To make sure that all parts of the mucous membrane are destroyed, the application of acid is repeated once or twice, after drying the sac each time. The cavity is then packed with aristol or bismuth formic iodide, which is left to absorb. Where there is much bleeding, or in the case of a large mucocele, it is well to pack the sac with iodoform gauze after opening it, not applying the acid until the next day, when a few crystals of cocaine in the sac will suffice for anesthesia.

In cases without marked dilatation of the sac, where the duct can be probed without much difficulty, *a trial of probing should usually be made before any operation is advised.* If great care is taken with the anesthesia for each probing a number of patients will permit a cure to be effected. After the first probing, which is carried out with large probes in the same way as was described for stenosis of the duct, an antiseptic such as 2 per cent mercurochrome or 1 to 1000 metaphen should be injected into the sac and through the duct. The next day an attempt is made to inject fluid through the duct, and if this is successful it is sufficient to inject a few drops of 10 per cent cocaine-adrenalin to shrink the mucosa so that the duct will remain patent for another day. On the second day, after the same injection, probing can be repeated with little or no pain, as a rule, and the antiseptic is instilled in the sac. Then the intervals of probing should be increased until the duct remains open without probing. If the secretion in the sac is viscid and the duct is found closed within twenty-four hours of probing it is necessary to repeat the probing and teach some member of the family how to wash a mild antiseptic solution through the duct two or three times a day between probings. If this is impossible and the duct is firmly closed within twenty-four hours after each probing the prognosis for a cure by this means is poor, and operation will usually be required. In such cases the use of a stilette which is left in the duct has been advised, and in some cases will produce enough atrophy of the duct wall to leave a permanent opening when it is removed after one or two weeks. Dean has described a silver tube which is inserted in the duct through a small incision over the sac, after curetting the sac and applying 2 per cent silver nitrate to its mucosa. He reports permanent cures after four or five probings with a No. 14 Ziegler probe, the tube being replaced each time and left for two days.

On account of recurrent swelling of the duct wall, occlusion by viscid secretion, or failure of the patient to coöperate, a

number of these cases are not relieved permanently by any method of probing, and in these cases operation must be advised.

After removal or obstruction of the sac some lacrimation persists, but it is much lessened by elimination of the infected contents of the sac which is effected by operation. If it causes much annoyance the accessory lacrimal gland may be resected or partial atrophy of the gland may be caused by injection of 1 cc. of 90 per cent alcohol directly into the orbital gland. In a number of cases, however, the effect of such an injection is slight or temporary. Such procedures are not without danger of causing deficiency in lacrimal secretion with resulting keratoconjunctivitis sicca, and are rarely indicated. The relief of epiphora as well as of the purulent secretion is, of course, the great advantage of dacryocystorhinostomy over excision or destruction of the sac and the reason for preferring it in most cases.

A common cause of epiphora is an anomoly in size or position of the lower tear-point, its gradual contraction in old age, or its eversion in the course of senile ectropion. While free slitting of the lower canaliculus for probing is never advised, *careful enlargement of the tear-point by two small right-angled cuts will often relieve epiphora of this type.* Sufficient anesthesia is secured by a pledget of cotton soaked in 10 per cent cocaine and left over the tear-point for five minutes. Then one point of a pair of a very sharp iris scissors is pressed into the dilated tear-point, and a cut made directly toward the conjunctiva, at right angles to the canaliculus. A similar cut is made along the course of the canaliculus, neither cut being over 2 to 3 mm. long. This allows the tear-point to gape (see Fig. 60), so that it is much larger, and the inner angle of the new tear-point dips into the lake of tears. These cuts must be gently separated by a blunt probe daily, after cocainization, until they remain open spontaneously, which is usually within four to seven days. In senile ectropion several cautery punctures through the conjunctiva close to

the tear-point, but without touching it, or a plastic procedure, will usually bring it into proper position, when it may be enlarged if necessary.

Occlusion of the common canaliculus is a not uncommon occurrence in old trachoma, and the pocket of infected material so formed is a cause of recurrent keratitis in patients with healed trachoma. Efforts to probe the canaliculus are unsuccessful, and methods of restoring its patency are very unsatisfactory. Morax's method of employing a Thiersch graft around a small peg is difficult and often unsuccessful. Goar was successful in one case by incising the sac and inserting a stilette back through the canaliculus.

Fig. 60—Right-angled incisions to enlarge lower lacrimal punctum. (Gifford, Textbook of Ophthalmology, courtesy of W. B Saunders Co)

To obviate the closed pocket formed by the canaliculi, which is usually swarming with bacteria and secretes a purulent discharge, it is only necessary to slit each canaliculus to its junction with the common canaliculus, converting the pocket into an open groove communicating on one side with the conjunctival sac.

Another less common cause of lacrimation and purulent discharge is the obstruction of one or more canaliculi by concretions of actinomyces or streptothrix. Such thread moulds, while not of the pathogenic type, offer a purely mechanical obstruction to the tears, which persists until the canaliculus is slightly slit and the ball of mould removed with a small spoon, this procedure being followed by irrigation through into the nose.

DISEASES OF THE LACRIMAL GLANDS.

Aside from tumors, disease of the lacrimal glands is rare. Besides the adenitis occurring during mumps, acute adenitis may occur without apparent cause, or in the course of a general infection. It is treated by hot packs and oral administration of the salicylates, incision being rarely necessary.

Symmetrical enlargement of the glands (Mikulicz's disease) is apparently usually due to tuberculosis or Boeck's sarcoid, is rare, and not susceptible to any but general treatment.

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CHAPTER XV.

DISORDERS OF THE MUSCULAR APPARATUS

CONCOMITANT CONVERGENT STRABISMUS.

While there is some difference of opinion as to the primary cause of squint, certainly *one important factor in the causation of this type of squint is the presence of hyperopia or hyperopic astigmatism.* Such errors of refraction are present in a large number of cases and would theoretically act to produce squint by requiring an excessive effort of accommodation. This function being intimately associated with that of convergence, such an accommodation excess is accompanied by an excess of convergence. Apparently, to avoid the diplopia resulting from such excessive convergence, one eye, usually the one having the highest refractive error, is turned in so that its image may be more easily suppressed. Hence in this condition *the first thing to be done is a careful refraction under complete cycloplegia.* In young children, as a rule, this can only be obtained by atropine, which is usually given the day before and several times on the day of the examination. In children over ten years of age the usual homatropine drops will usually be sufficient. Children should be refracted as soon as squint develops, since the earlier this is done, the greater is the chance that it may be corrected by glasses. With babies, one to two years of age, retinoscopy can usually be carried out with a little patience, and the idea widely current even among some physicians that nothing can be done for squint until the child is old enough for a subjective test should be opposed at every opportunity. In such cases retinoscopy is absolutely essential, subjective tests in children under ten years of age being notoriously unreliable, and in those under seven years usually impossible. If

retinoscopy is impossible in certain babies refraction with the ophthalmoscope under light general anesthesia and cycloplegia should be carried out. If hyperopia or hyperopic astigmatism is discovered this should at once be corrected by glasses for constant use. The higher the hyperopia, the greater the chance of correcting the squint by glasses, and the correction prescribed should be as near the full correction under cycloplegia as will be tolerated. If the hyperopic error is less than 1 diopter bifocal glasses, with +2.50 added in the reading segments, are usually prescribed for children of school age. Where emmetropia, or even slight myopia, is shown by the examination the refractive error may be excluded as a cause of the squint, there is no indication for the use of glasses, and other measures may be begun at once.

If one eye is amblyopic, or is constantly convergent, occlusion of the fixing eye should be practised, not only to aid in correcting the squint, but to develop function in the squinting eye The prospect of improving function in such eyes is greater in young children, below the age of five or six years. When a case is first seen at the age of eight to ten years there is much less chance of this, but a trial of occlusion is indicated, while after the age of twelve years improvement in vision is seldom if ever observed.

Occlusion is usually carried out for an hour or more a day by placing a pad of cotton under the glasses, held in place, in young children, by adhesive tape. This is undoubtedly superior to the use of atropine in the fixing eye, which is of little effect except in cases of very slight amblyopia. If the vision in the squinting eye is very poor, below 10/200, occlusion will be very difficult to carry out, and demands much persistence on the part of the parents, but an attempt to carry it out should be made. Where possible, which is usually in cases without such marked amblyopia, complete occlusion of the fixing eye by a fixed dressing for periods of several weeks or months, repeated at frequent intervals, is certainly the most effective way to improve vision in ambly-

opia. Although the results are often discouraging and will be negative in many instances, enough cases have been reported showing a definite improvement in vision by these methods to justify a trial in every case. Uhthoff insisted on the great value of prolonged constant occlusion, and reported some apparently remarkable instances of improvement in vision. In alternating squint, where vision is the same in both eyes, alternate occlusion is advised in an attempt to remedy the false projection existing in such cases. To be effective it should really be continued constantly except for periods of orthoptic exercise until the eyes are made parallel either by refractive correction or surgery. In the author's experience *this is the only way in which fusion can be developed in cases of squint with false projection*, which exists in at least one-third of the cases of concomitant strabismus. The idea of alternating occlusion is that of preventing use of the area of false fixation which exists in these squinting eyes when in the anomalous position.

The *use of atropine in the fixing eye* is employed by many ophthalmologists as a substitute for occlusion. It is of value chiefly in patients without extreme amblyopia, since where vision is reduced below 20/70 in the squinting eye, the vision of the fixing eye under atropine will still be superior to it, and fixation with this eye will be continued. Where vision is only slightly reduced in the squinting eye, atropinization of the fixing eye or overcorrection of this eye enough to reduce its vision below that of its fellow is often of value.

Unless the proper correction has been worn before one sees the patient, a trial of glasses worn constantly for a year or longer should be made in every case showing refractive error, and especially in children, before operation is considered. In about one-half the cases of children showing any considerable amount of hyperopia glasses will improve the squint markedly and in many cases will correct it entirely while the glasses are worn. Whether it is justifiable to operate in such cases so the glasses will not be required is

rectus should never be performed in a child on account of the danger of later divergence. This danger is especially great if tenotomy is performed at the same time as shortening of the opposing muscle, since the resulting attachment of the tenotomized muscle may be so far back that all power of convergence is lost.

Once the squint is corrected, or nearly corrected, by operative means, orthoptic training should be continued rigorously, and if this is done binocular vision should be obtained in nearly all patients unless amblyopia of one eye is too extreme and unless false projection is present. Such exercises are especially important in cases which had previously shown alternating convergent squint, since here there is a tendency to recurrence of the squint unless fusion can be obtained.

CONCOMITANT DIVERGENT STRABISMUS.

In this condition *the presence of a refractive error is undoubtedly of less importance than in convergent squint.* Where myopia is present it may theoretically be of importance in that near vision is accomplished without an effort of accommodation, and hence the normal amount of convergence which accompanies normal accommodation is not brought into play. A careful refraction under cycloplegia is indicated as in convergent squint, and where myopia is found the use of glasses may be of value, since with glasses a normal accommodative effort for close work is required. Practically, however, the use of glasses alone in such cases seldom results in correction of the squint.

Amblyopia is a far more important factor, and this may be due to marked anisometropia, or to defective development of the central retina from any cause. The indistinct image of such an eye is apparently suppressed, and the eye seeks the position of rest, which is usually one of divergence and slight sursumvergence. *Under such conditions anything* which will improve the vision of the amblyopic eye and

stimulate fusion will be of possible value in correcting the squint. Occlusion of the fixing eye combined with orthoptic exercises should be given a trial in such cases whenever possible. The amblyopic eye should, for these exercises, be fitted with its proper correction where a definite refractive error is present. The cases in which most can be expected from these procedures are those of latent divergence, in which parallelism of the eyes is present during part of the time. Fusion may be present in these cases and the object of exercises is to bring about a consciousness of diplopia when divergence occurs, so that it will be avoided. The use of orthoptic exercises in this condition will be described later.

When improvement is being obtained by occlusion and exercises they may be continued as long as this progress goes on. If fusion is present during part of the time spontaneously, or is obtained during exercises, there is not the same indication for early operation as where squint is continuous. *When it is apparent that no more progress is being made, however, and the squint remains uncorrected, there can be no reason for delaying operation.* Advancement and recession on the squinting eye are usually necessary and in some cases advancement of the opposite internal rectus may later be necessary.

Orthoptic Exercises.—The use of occlusion of the fixing eye in an effort to develop function in an eye previously amblyopic has been described and some of its limitations have been mentioned. Where an anatomical defect in structure is present which accounts for the poor vision no result may be expected from such training. Also, as has been stated, where the amblyopia is of long duration occlusion is ineffective in improving vision. Where the amblyopia is of extreme degree, with vision of only hand movements, it may be impossible to carry out monocular occlusion systematically. And in many apparently favorable cases no improvement is obtained. In spite of these limitations, an attempt to improve vision by this means should be carried out wherever the necessary coöperation can be secured.

The same remarks apply to the use of the various types of orthoptic exercise which attempt to develop the fusion sense. Where the amblyopia of one eye is extreme the images used in the various exercises cannot be perceived well enough so that exercises can be performed. In very young children and in mentally defective children the necessary cooperation cannot be obtained. Children vary greatly in this respect, and while some children may carry out certain exercises at the age of five, or even four years, it is usually children of

A *B*

Fig. 61.—*A*, Convergent strabismus before treatment, *B*, after seven months orthoptic training.

six to eight years of age who can be counted on for this purpose. Older children coöperate more readily in training and *even in young adults who have squinted since infancy it is often possible to develop binocular vision.* (Fig. 61.) Where the squint is of high degree, over 30 degrees, the prospect of relief by orthoptic training is much less than in squint of 15 degrees or less, and in such cases it will often be best to operate early and take up training after operation.

For practical details of orthoptic training and for a report of results obtained, reference is made to the articles of

Guibor, Peter and others. *Before beginning treatment a careful examination should be made.* Vision should be recorded with the best correction after careful refraction under a cycloplegic, and the amount of squint present both with and without correction should be recorded in degrees of the perimetric arc. Where the squint is slight the strength of prism required to superimpose the two images should be determined with the Maddox rod or the red glass over one eye, where this is possible. The prisms may be added in the trial frame or by means of the phorometer. In most cases of squint only one or the other image is seen at the same time, so that this test cannot be employed.

The *amblyoscope of Worth* may then be tried. This instrument makes use of two movable tubes through which complementary pictures are seen and superimposed by moving the tubes. In some cases of squint this may be achieved without the use of prisms. In others prisms will be required which are used with bases in for divergent and bases out for convergent squint. Where one eye is amblyopic this procedure is accomplished only with the use of a strong light before the tube corresponding to the amblyopic eye, since the pictures are on transparent screens, and this brings out the more indistinct image. In many cases, however, none of these procedures will enable the patient to superimpose the images, as when one image is seen the other is suppressed, especially when it comes close to the superimposed position. In these cases the use of the amblyoscope for exercises is naturally impossible, and should not be attempted until improvement of vision by occlusion or correction of the squint by glasses or operation has changed conditions so that the patient is now able to superimpose the images. Even then, in too many cases such an amount of fusion is still impossible.

An instrument devised by Maddox, and called by him the *cheiroscope*, makes use of the principle that moving objects produce a stronger stimulus to the amblyopic eye and also employs the coördination of eye and hand in developing

fusion. By means of a movable mirror the image of one eye, no matter what its position, may be superimposed upon that of the other. Thus a picture on a rotating plate is reflected upon a drawing-board which is apparently seen by the other eye, and after its movement has caused it to be fixed by the amblyopic eye, it is held stationary and traced upon the board. When the mirror is placed so as to divide the drawing-board vertically into two fields part of these are seen by both eyes, and small toys or other objects which have the advantage of being solid, and so stimulating depth perception, may be moved with both hands so that their images are superimposed and fused. Such fusion may be accomplished by patients who cannot use the amblyoscope, in which the flat pictures are not fused so readily, and, according to Maddox, much may be done in the reeducation of such patients. An American instrument similar to the cheiroscope is now available.

Other useful instruments are the *Synoptophore* and *Synoptiscope*, both of which allow superposition of images in extreme degrees of squint, making use of the principle of the amblyoscope. If a patient can be taught to fuse with one of these instruments, it usually becomes possible before long to employ the *stereoscope with suitable prismatic correction*, which can be employed at home.

For patients who prove to be capable of using the stereoscope, as shown by their ability to fuse the pictures either with or without prisms, a course of exercises with this instrument affords the simplest and least expensive form of orthoptic training and one which is probably as effective as any other.

A number of charts are available for use with the stereoscope, *those of Wells, Sattler and Guibor being especially useful*. In the two latter series the charts are split so that they may be moved variable distances apart, and by reversing the charts a reverse picture as regards depth impression is obtained. **(Fig. 62.)**

Two matched pictures are placed in the holder at such a distance from each other that they can be fused with the slide at about the middle position. The slide is placed nearer or farther than this position and the child is asked to move it closer or farther until the pictures are fused. One part of the fused picture, such as a ball hanging in a ring, will then

FIG 62 —Guibor's split-charts for orthoptic training

appear either nearer or farther away than the rest of the picture, and the patient is asked in which of these positions it is seen. This is checked by the parent, and if correct the positions of the cards are changed from right to left, when the positions of the parts in space will appear reversed, that is, the ball which was previously seen nearer, is now farther away than the ring. The procedure is repeated with other

pictures, the exercises being continued from five to fifteen minutes, and repeated three times a day. When the Wells charts are used the pictures of Series A are first used, the missing parts of one picture being supplied by those of the other when fusion is obtained. When this series is completed Series E may be used, in which the fused pictures represent solid objects which should be seen as such. A bucket, for instance, when the two pictures are fused, is seen as hollow with the bottom farthest away. After this, if the child can read, Series C is taken up. This is a series of reading exercises, in which portions of letters or words are defective in one picture and must be supplied from the other. Larger print is read first, proceeding to smaller print, where the vision of the poorer eye will allow of its use. For further details as to the use of these charts, the reader is referred to Wells' book on the stereoscope.

Where the stereoscope cannot be used, but the pictures of the amblyoscope can be fused, this instrument should be used. It should be bought or rented for the patient, since to be effective the exercises should be performed several times daily, and this can usually be done only at home. With this instrument the pictures are of the same type as Series A of the Wells charts, and the patient is asked to form a complete picture by approximating or separating the tubes, until for example, he has put the bird in the cage, or the hands in the clock. They are then separated and replaced in position several times before the next picture is tried. If prisms are at first necessary they may be placed in the holders on the tubes, and their strength is gradually decreased until fusion is obtained without them, which should also be carried out with the stereoscopic exercises. When this can be done, and the series of pictures has been gone over many times, it is well to begin the use of the stereoscope if the patient can now use this instrument. Exercises with the amblyoscope should be conducted for about the same periods and at the same intervals as those with the stereoscope, the patient being

seen by the physician every few weeks or every month in either case to make sure that the exercise is being properly carried out.

In younger children or those who cannot use the amblyoscope, exercises with the cheiroscope may be tried. These must usually be conducted in the office, since the instrument is somewhat too expensive for purchase by most patients. For the busy ophthalmologist a nurse or assistant trained in the use of these exercises will be almost a necessity if office exercises are to be carried out. In some cities, such as London, New York and Chicago, centers have been established for orthoptic training under specially trained persons, and probably the best result may be obtained in such centers; provided a proper check is kept by the ophthalmologist on the patient's progress.

It should be repeated that the use of any of these methods requires great patience and not a little intelligence on the part of the patient, parents and ophthalmologist. In many cases which seem suitable for the exercises they will be abandoned because of lack of patience. To produce a permanent effect they must be continued over periods of six months to a year or even longer, until fusion becomes instinctive, and any temporary absence of it causes troublesome diplopia. In a number of cases even after earnest efforts to carry out the exercises it will be apparent that no progress is being made, and the ophthalmologist should be the first to recognize this fact. The more care is taken, however, in choosing suitable exercises, and instructing patients in their use, the more good results will be obtained. Such results are especially important after strabismus has been corrected by operation, and one is often surprised to find patients up to the age of twenty or thirty years who acquire useful stereoscopic vision by the combination of surgery and orthoptic training.

The experience of a number of years with orthoptic training has modified, in some respects, the hopes entertained for the

method. This modification applies especially to the large group of *patients with anomalous correspondence* who often persist in suppressing vision in the true macular area of the squinting eye even when this is made parallel by surgery. It is much more difficult to maintain exact parallelism in such cases, and the development of habitual binocular vision is exceedingly difficult. *Prolonged alternate occlusion in such cases, with adequate surgical correction at an early date*, seems to be the most important measure in combating this condition.

VERTICAL STRABISMUS.

Where not due to actual muscle paralysis, this is usually an accompaniment of convergent or divergent strabismus, the deviating eye turning usually up and out or up and in. It is usually corrected by the same measures as are employed for the horizontal squints, but may have to be considered in the operative treatment of these defects. *Orthoptic training is of no value in pure cases of vertical strabismus, until surgical correction has been accomplished.*

HETEROPHORIA.

In this group of conditions *no actual squint is present*, and the fusion faculty is well developed, *but due to either spasm or weakness of a muscle or group of muscles there is a latent tendency to divergence, convergence or sursumvergence* which allows the act of fusion to be performed only in response to an abnormal effort. This effort often causes symptoms of eye-strain, and when it is relaxed during periods of fatigue, actual diplopia may occur. Its presence is usually revealed by tests with the Maddox rod, and its degree is determined by the strength of prism required to superimpose the two images which are seen when fusion is suppressed by the presence of the rod over one eye. The question which group of muscles is at fault, and whether the condition is one of spasm or weakness, is determined by duction tests for each

group of muscles, the amount of prism being recorded with which fusion can still be accomplished when the prism to be overcome is placed in various directions. For this purpose a phorometer is most convenient, but prisms in the trial frame may also be employed. Perfect muscle balance is unusual, 2 to 3 degrees of esophoria or ½ to 1 degree of exophoria being very commonly present and being tolerated, as a rule, with no symptoms whatever. Vertical phorias, however, are more likely to cause symptoms, and the presence of over 1 degree of vertical phoria or a greater amount of horizontal phoria than those mentioned may call for treatment, where the refractive error is already perfectly corrected and no other cause for the symptoms is to be found.

The most rational method of treating the phorias is the *attempt to correct the muscular imbalance by exercises or, in rare cases, by operation.* The simplest procedure and that most often employed where glasses are worn, is the adjustment of the correction to aid in correcting the phoria. If esophoria is present this is usually ascribed to a spasm of convergence due to excessive accommodation, and the full correction of all hyperopia revealed under cycloplegia or a slight overcorrection of this for reading may be of great help in relieving symptoms from this cause. Where the opposite condition of exophoria is present the full correction of myopia or an undercorrection of hyperopia may be of some assistance, but this less often proves to be the case.

The use of *exercises in overcoming prisms with bases out,* according to Gould's method, has frequently been employed in exophoria and often with considerable effect. The average person can fuse while wearing 12 to 14 degree prisms bases out over either eye, and for patients who can overcome only 6 to 8 degree prisms a course of exercises with prisms of increasing strength up to 20 for each eye may give results. In the author's practice ten sets of prisms from 2 to 20 are loaned to the patient, beginning with the set with which fusion is just possible at one foot. The patient is instructed to fix a

small white card at this distance and walk backward to a distance of 20 feet or until diplopia occurs. When this occurs he approaches the object until it can be fused and repeats the process. When fusion is easily accomplished at 20 feet the next set of prisms is substituted, and this is repeated until fusion is possible with a 20-degree prism over each eye. Exercises are continued for a few minutes twice a day until this can be accomplished, and the use of the 20-degree set is continued once a day for several weeks. This method is of use in some cases of asthenopia even without marked exophoria in patients who will coöperate intelligently. In other cases it proves of little or no effect.

For the vertical phorias and esophoria the same method may be employed, as described by Berens and Losey, or stereoscopic exercises may be carried out while overcoming prisms of increasing strength, the prism being directed so as to place an increasing demand on the supposedly weakened muscle, base in, for example, in esophoria and base up over the right eye for right hyperphoria. The use of the phorometer to increase duction in the various directions has the same effect, but this necessitates such frequent office visits, if it is to be effective, that it is practicable in but few cases.

While these methods are logical, they are nevertheless often ineffective, and it is often impossible to carry them out. *Much simpler is the opposite procedure of supplying the supposedly defective action of a group of muscles by a prism for constant use or for use in close work.* Here the prism is placed in the opposite sense to that used for exercises. In exophoria, for example, prisms bases in of sufficient strength to correct the latent imbalance may be used. Usually it is sufficient if these be prescribed for close work, either in half-fronts or in separate glasses, and those who have employed this method will agree that it often produces complete relief of symptoms. Contrary to what might be expected, the use of this "crutch" does not weaken the assisted muscles so as to increase the phoria, as Dean showed in a series of cases followed for years.

may be mistaken for concomitant convergent squint unless care is taken.

In paralysis of the vertical recti or of the obliques advancement of the partially paralyzed muscular or recession of its synergist will, if the proper procedure is selected, usually abolish diplopia in a greater part of the field. In some cases the constant use of prisms will be preferred.

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CHAPTER XVI.

DISEASES OF THE ORBIT.

ORBITAL CELLULITIS.

Infection of the orbit arises from the blood stream in the course of general infections, from furunculosis or erysipelas of of the face, or from the neighboring para-nasal sinuses. Treatment will depend upon the origin of the infection and upon the stage at which the case is seen. Prompt and careful rhinological examination is indicated in every case, including roentgenograms of the sinuses and orbit. If definite infection is discovered in the sinuses, provision of adequate drainage by anemization of the nasal mucosa or if necessary, by surgery, may result in resolution of the orbital infection, and should not be delayed. In other cases of nasal origin an abscess has already begun to form in the orbit which must be treated locally in addition to the nasal treatment required.

In cellulitis not of nasal origin, treatment will depend upon the stage of the infection. If the case is seen early, *heat is applied as constantly as possible.* The use of the infra-red lamp during the waking hours with three or four half-hour periods of rest is probably the most efficient method in such cases. Moist hot packs require the constant care of a nurse and cannot be kept hot enough to deliver the desired amount of heat.

The effect of short wave diathermy may, in some cases, be preferable to that of the heat lamp. In early cases and even in some later ones, the use of *the sulfonamides* has not infrequently been responsible for resolution without incision of the orbit. When secondary to erysipelas, or of unknown origin, *sulfanilamide* in full therapeutic dosage (see page 102) is indicated, while when cellulitis follows a staphylococcic infection of the skin, *sulfathiazole* will be preferred. Use of

these drugs, while often successful, should not allow delay in the care of infected paranasal sinuses or in drainage of an abscess when the indications arise.

When a case is seen several days after the onset of inflammatory symptoms, it is likely that an abscess has begun to form, in which case *prompt incision and drainage is indicated.* It may be difficult to localize the abscess, though fluctuation and lateral displacement of the eye or limitation of motility in one direction are useful guides. Incision must be deep in the orbit, and is best performed under light nitrous oxide anesthesia. If pus is not found at the first incision it may be necessary to make one or more additional incisions. The orbital wall should be reached and the periosteum opened, as an abscess often begins beneath it, especially when it arises from the para-nasal sinuses. In a few cases the abscess is inside the muscle-cone, and this must be opened and drained. Incisions at the margins of the orbit, especially just below the brow, leave inconspicuous scars, and should be large enough to permit adequate drainage. After the superficial tissues are incised a large grooved director is useful to explore further into the orbit and this avoids unnecessary bleeding. If a free flow of fluid pus is obtained, drainage will usually be sufficient if the wound is opened daily for several days by a probe, heat being applied in the meanwhile. If the pus is very thick and flows with difficulty it will be necessary to enlarge the deeper parts of the incision and insert a U-shaped drain of silver-wire which may be removed daily.

In an occasional case no localized abscess forms. The cellulitis remains diffuse, or forms numerous micro-abscesses in the orbital spaces. Here there is great danger that infection may spread to the cavernous sinus and it may be necessary to eviscerate the orbit to prevent this. In a case of the author's the entire orbital contents were converted to a beefy mass which resembled a piece of liver on section and contained innumerable minute abscesses. In such a condition orbital evisceration is necessary to save life. Enucleation of the eye

most cases, following relief of this by surgery or other means, the exophthalmos gradually recedes until a normal or nearly normal condition is re-established.

In a certain number of cases, however, the exophthalmos is so marked that protection of the cornea is required. The moist chamber of roentgen-ray film described in Chapter VIII is most useful here. Often this and the use of a mild antiseptic to cleanse the conjunctival sac are all that is necessary until

Fig. 63.—Extreme exophthalmos in hyperthyroidism.

the effect of medical or surgical treatment is obtained. The beginning of keratitis constitutes, of course, an urgent indication for such treatment.

In other cases, however, the conjunctival chemosis becomes worse (See Fig. 63), paralysis of one or more ocular muscles occurs, and vision begins to suffer through pressure on the optic nerve, even while the cornea is still clear. *This form of malignant exophthalmos is especially apt to occur in those cases in which exophthalmos first appears or becomes worse following*

thyroidectomy. Naffziger has studied this condition most thoroughly and has found a marked swelling and inflammation of all the extra-ocular muscles which he believes is the principal cause of the exophthalmos. His method of *decompressing the orbit* by removing its bony roof from above after craniotomy has now proven successful in a number of cases. The corneas are preserved, the nerves assume a normal appearance and much or all of the vision is restored. The exophthalmos, while seldom disappearing entirely, becomes appreciably less. In the hands of a neurological surgeon who is familiar with the method, there should be no mortality from the operation itself, while in cases which are allowed to go on until both eyes are lost by panophthalmitis, the mortality is exceedingly high.

Another method of decompressing the orbit is by the *Kronlein method* in which the lateral wall of the orbit is resected. A number of ophthalmologists have preferred this method, and report results equal to those of Naffziger, though no reports so complete as those of Naffziger have appeared. Attempts to decompress the orbit by removing fat are usually unsuccessful, since the operative disturbance in the orbit itself produces an edema which may be fatal to the cornea. It is usually impossible to suture the lids over the cornea in the presence of such marked exophthalmos.

INJURIES OF THE ORBIT.

After any penetrating wound of the orbit, a roentgenogram should be made to determine the possible presence of an intraorbital foreign body. Objects which are not radio-opaque are often over-looked, but the presence of localized swelling should arouse suspicion and exploration in the region of the wound will often reveal a fragment of wood or some other substance which should be promptly removed. Objects near the apex of the orbit are best reached by a Kronlein incision and the prompt removal of foreign bodies by this method will often avoid serious cellulitis and damage to the optic nerve or extra-ocular muscles. Small foreign

bodies which are causing no symptoms of inflammation or pressure on the nerve may safely be left alone.

Orbital Hematoma following injury calls for cold applications which should be continued until the danger of fresh hemorrhage is over and the swelling has subsided. Occasionally hemorrhage is so severe that marked exophthalmos develops and the cornea or optic nerve is endangered. This may call for prompt decompression of the orbit by the Kronlein method, since the removal of blood by an orbital incision is unsatisfactory and likely to cause fresh bleeding.

Fractures of the Orbital Walls should be detected by roentgenogram after any severe orbital injury. When the fracture involves the optic foramen with loss of vision by pressure on the nerve, prompt decompression of the orbit by the Naffziger method will occasionally be successful in restoring or preserving some useful vision. Usually the case is seen when it is too late for this procedure, which must be done very soon after the injury.

Pulsating Exophthalmos results occasionally from a penetrating wound which injures the carotid artery in its course through the cavernous sinus. It also occurs following rupture of an aneurysm in this location. When the head-noises which result are severe, or when the vision decreases as a result of pressure on the optic nerve, operative interference may be necessary. Digital pressure on the common carotid usually relieves symptoms considerably and when this is maintained by a special appliance a number of patients are relieved. Of Sattler's 83 collected cases, 12 obtained complete and 22 partial relief. *Permanent relief is obtained in a larger proportion of cases* (67 per cent according to Birch-Hirschfeld) *by ligation of the common carotid artery.* This should be done only after periods of compression to avoid the effect of sudden cerebral anemia. It is not entirely without danger, but this is slight if proper precautions are taken. Ligation of the internal carotid has also been frequently employed, but the results are less often completely successful. (47 per cent according to Birch-Hirschfeld.)

CHAPTER XVII.

INJURIES OF THE GLOBE.

While a large number of ocular injuries require hospitalization and surgery, there are a number of cases in which first aid or minor procedures may and should be carried out whereever the case is first seen.

The removal and after-care of *foreign bodies in the cornea* has been discussed in Chapter VIII. The important thing is to recognize at the outset infections of the cornea resulting from foreign bodies and treat them by the methods described for corneal ulcer.

CHEMICAL BURNS.

Chemical burns of the conjunctiva and cornea should be treated at once by *copious irrigation with any clean nonirritating solution*, care being taken that the folds are well everted so that the whole surface of the conjunctiva is thoroughly cleansed, and no particles of lime or other chemical remain adherent to it. The dispatch with which such irrigation is applied is much more important than the kind of solution used, which may be water, normal saline or a saturated solution of boric acid. After this irrigation there is time to ascertain the nature of the chemical.

Alkali burns seem to heal more promptly when *1 per cent acetic acid* is used freely in the conjunctival sac. This, as Hubbard has pointed out, is because the alkaline proteinates formed in the tissues are soluble and continue to produce damage unless neutralized. The proteinates resulting from *acid burns*, on the other hand, are insoluble and are not affected by neutralization after the free acid is removed by irrigation. It was the impression of Hubbard and Culler that acid burns heal better when treated only with water or

neutral solutions. If any attempt at neutralization is made, a 3 per cent sodium bicarbonate solution is the strongest alkali which should be employed.

Lime burns, after irrigation, may well be treated with a freshly prepared 5 or 10 per cent solution of neutral ammonium tartrate. This forms the soluble calcium tartrate and hence allows removal of lime from the tissues. According to the Barkans, it should be instilled freely several times a day for a week or longer.

Burns with tear gas (chloracetphenone) should be treated promptly, according to McNally, with solution of *sodium sulphite.* For burns of the skin he employs a 50 per cent alcoholic solution. For burns of the conjunctiva and cornea a 0.4 per cent solution is employed, 0.4 gm. of sodium sulphite being dissolved in 25 cc. of water and 75 cc. of glycerin. Instillation of the solution is repeated several times a day for several days. In the absence of sodium sulphite, McNally advises the use of glycerin, since tear gas is soluble in glycerin though less completely than in solution of sodium sulphite. He believes the absorption of water from the tissues by glycerin is of value in lessening chemosis after burns with tear gas and a number of other chemicals.

Burns with sulphur dioxide are seen chiefly in persons working on mechanical refrigerators. The damage is largely due to rapid evaporation of the liquid resulting in a *freezing injury.* Sulphurous acid is also formed in the tears which adds the trauma of an acid burn. The only treatment is prompt irrigation with water and the subsequent protective measures advised after any burn. Culler has pointed out that certain new refrigerants are being employed to replace sulphur dioxide and that burns with these substances require different treatment. Dichlor-difluor-methane (F. 12) and dichlor-tetrafluor-ethane (F. 114) are insoluble in water but miscible with oil. Hence the use of water is contraindicated and repeated instillation of olive oil is advised.

Water should also be avoided after burns with *mustard gas* since this is active only in the presence of water. Protection against mustard gas would hence include the use of bland oil in the eyes and a thick ointment on the face, including the lids. When the burn has occurred, McNally advises using glycerin to remove any free chemical.

Burns with *heat, formalin,* or other chemicals not previously mentioned may be treated only by irrigation and protective measures.

Following any burn a drop of fluorescein will reveal the extent of damage to the corneal and conjunctival epithelium. A prognosis as to the probable visual damage may be approximated by the depth of staining and depth of opacity in the cornea. The appearance of white areas of sclera indicating complete destruction of the conjunctival vessels is a bad prognostic sign, since absence of nutrition to the cornea results and is followed by progressive opacity and later vascularization or even by sloughing of the entire cornea. Extensive staining of the conjunctival epithelium is an indication for special care to prevent partial or complete symblepharon. Olive or castor oil should be instilled frequently and when adhesions occur they should be separated several times a day with a smooth probe. *Deep burns of the conjunctiva are best treated,* according to Thies, by *immediate grafts of mucous membrane* from the lip, after removal of necrotic conjunctiva. Such grafts offer a pathway for ingrowth of new vessels which prevent later necrosis of the cornea. Thin grafts will often heal in place even on a badly necrotic surface, according to Thies. Pain is severe after burns of the eye and use of a local anesthetic is often necessary. Cocaine should never be employed, but 0.5 per cent butyn or holocaine causes little or no damage to the epithelium, and may be used several times a day. An ointment of 1 per cent butyn or holocaine or 0.25 per cent pontocaine may have a more prolonged effect.

CORNEAL EROSIONS.

After any contusion to the globe it is well to instill a drop of 1 per cent fluorescein, which will often reveal a loss of epithelium of considerable extent. The only treatment required for such an erosion, as a rule, is to keep the eye under a dressing until healing has occurred, which is usually within twenty-four to forty-eight hours, and the use of a local anesthetic, such as butyn or holocaine, to lessen the pain, which is often very severe. One-half to 1 per cent butyn or holocaine, in solution or ointment, may be used as often as is necessary to control pain. Cocaine should not be used for this purpose, as it tends to delay regeneration of epithelium

A not uncommon complication of chemical burns or even very slight corneal abrasions is the development of *recurrent corneal erosion*. Apparently certain persons are predisposed to this condition, while in other cases a certain type of injury such as the abrasion of a finger-nail or a drop of ether received in the eye during anesthesia appears to produce a type of damage to the corneal nerve endings which results in recurrent erosion. In this condition the original area is rapidly covered with epithelium, but this adheres only loosely to Bowman's membrane. Fluid collects beneath the new epithelium, forming a bleb, and also penetrates beneath the surrounding epithelium, so that almost the whole corneal epithelium becomes loose enough to be easily peeled off with forceps. (Fig. 64.) When the bleb ruptures severe pain is felt, the loose epithelium is cast off and the process is repeated. Apparently loosening of the new epithelium is favored, or actually brought about, by opening of the lids to which it adheres more firmly than to Bowman's membrane. Very suggestive of such a condition is the history of sudden pain during the night or on awakening in the morning. This may occur weeks or months after a slight injury or removal of a foreign body when the original injury has often been forgotten entirely by the patient. Such attacks may recur at

Once a recurrent erosion has developed, it is best to apply radical measures to stimulate firm healing. The only effective means of doing this, apparently, is *the complete removal of all loose epithelium from the cornea with forceps*, and this will often include practically the whole surface of the cornea. This is followed by a careful application of an astringent to the entire denuded surface. Freshly prepared aqua chlori was advised by von Szily, but the author has found 10 to 15 per cent trichloracetic acid as effective. In spite of one's fear of causing opacities with this acid, these have not occurred, and its use apparently promotes firmer attachment of the new epithelium to the cornea.

Emptying of the anterior chamber by a subconjunctival paracentesis seems a logical procedure to hasten normal healing, and though it may be superfluous, has been performed just after the application of acid in the author's cases. This is followed by a *binocular dressing which is kept in place for four days*. The eye is then opened very cautiously after allowing a little 2 per cent butyn solution or olive oil to moisten the cornea from the lid-border, as it is the first removal of the lids from the cornea which is feared. Usually the epithelium is found to be smooth and firmly attached, and after a dressing for twenty-four to forty-eight hours longer, no more care is required. Scars in the stroma never result from this procedure, apparently, and vision returns to normal unless the condition had recurred many times before this treatment was undertaken, when some scarring may be left.

In uncomplicated recurrent erosion this procedure is nearly always effective and prevents further recurrences. In a few cases, especially when the erosion occurs after uveitis, penetrating wound, or cataract operation, or following tonometry in an eye with glaucoma, it is ineffective and is followed by fresh erosions. *In such cases the procedure must be repeated*, with removal of every shred of loose epithelium, and *in addition the lids must be kept closed for long periods*. This is best

done by producing a *single central adhesion between the lids* according to Wheeler's method. Opposing areas are denuded with a cataract knife and sutured firmly in opposition. (See Fig. 53.) The adhesion stretches within ten days so that the eye may be inspected but it is usually well to leave it in place for two to three months when healing is firm enough to allow the adhesion to be cut.

Small localized erosions of the cornea or conjunctiva which occur repeatedly in the same place should suggest a search for local causes of irritation. Small *lashes touching the cornea* are easily overlooked unless the lid-borders are carefully examined with the loupe in good light. When one such lash is discovered it may be epilated with forceps, but the patient should be warned that it may recur. If this happens, the lash follicle should be destroyed by electrolysis or diathermy coagulation. If many inturned lashes are present, an operation for trichiasis is the only satisfactory procedure. One occasionally sees an erosion persisting for a number of days as the result of a lash having lodged in one of the canaliculi with a short end protruding. Removal of the lash gives prompt relief. *Small pieces of vegetable matter*, especially hooks of certain burrs sometimes become imbedded in the conjunctiva and irritate the cornea or conjunctiva till they are removed. When deeply imbedded they form small granulomata which require excision.

In a number of cases the author has observed a condition which may be called *micro-recurrent erosion of the cornea*. A history of repeated nightly attacks of pain is given, following a trivial injury. The cornea looks normal on gross examination, but with the slit-lamp an irregular ring of very fine opacities is seen in the corneal epithelium. (Fig. 65.) Soon after an attack of pain one or more of these areas stains with fluorescein while during quiet periods no staining is present. In such cases no loose areas of epithelium are found but healing in certain minute areas is apparently imperfect. The condition is often very obstinate but can usually be con-

trolled by touching each tiny area which stains very carefully with 50 per cent trichloracetic acid and by the instillation of olive oil every night for long periods.

LACERATIONS OF THE CONJUNCTIVA AND LIDS.

Unless signs of infection are already present, *these should be repaired at once, the edges being opposed as accurately as possible with fine silk*, since after cicatrization has occurred

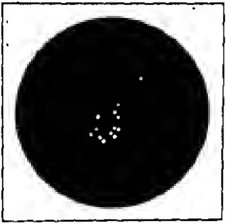

Fig. 65.—Micro-recurrent corneal erosion.

this is much more difficult to accomplish. The wounds should be washed carefully with a sterile solution, half-strength tincture of iodine applied to the involved skin and a mild antiseptic instilled freely in the conjunctival sac. Before suturing a laceration of the lid the retrotarsal fold should be thoroughly examined, as it is easy to overlook injuries here which, unless repaired, will cause symblepharon. The extent of orbital involvement must also be determined, as one or more ocular muscles may be severed or the bones of the orbit fractured by an injury which appears relatively

apposition. Atropine is usually given after any penetrating wound, to free the iris from the wound and to insure dilatation of the pupil in case iridocyclitis develops. In special cases of small peripheral wounds with a button of iris partly included it may be possible to free the prolapse with a spatula after

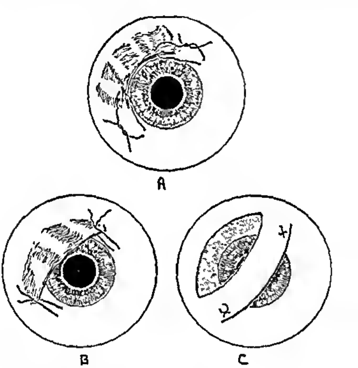

FIG. 66.—Technique of preparing conjunctival flap. *A* and *B*, sliding flap. *C*, bridge flap. (Gifford, Textbook of Ophthalmology, Courtesy of W. B. Saunders Co.)

use of a miotic instead of excising it. This is only advisable if it is performed within a few hours of the injury. Later than this the possibility of carrying bacteria into the eye is so great that the iris should not be replaced.

After any penetrating wound of the globe, and especially one requiring conjunctivoplasty, *it is important to keep the*

eye under a rigid shield to prevent reopening the wound by an unforeseen movement or a bump with the hand during sleep. For this a number of the masks devised for use after cataract operation are useful. A practical model which can be made to fit any patient, is shown in Fig. 67. It is made from glazed fiber board, but any thin strong cardboard will serve the purpose. The points may be held together by the brass clips used for notebook paper, in case the Hotchkiss or

A

B

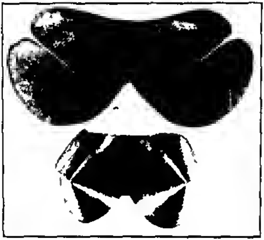

FIG 67.—H Gifford's cardboard shield for use after injuries or intraocular operations. *A*, Flat cut-out of shield; *B*, complete shield.

some other mechanical clipping device is not available. The projection over each eye should be made prominent enough so that plenty of space is left between it and the dressing.

After any penetrating ocular injury the danger of infection is always present, and when any case is first seen there is usually some uncertainty as to whether or not this complication will develop. An injection of foreign protein sufficient to cause a good febrile reaction is indicated because of its possible value in preventing this complication. Where antitetanic serum is indicated this will serve the same pur-

pose if enough serum is given, while in other cases it is a good routine to give 30 million typhoid bacilli intravenously.

If signs of infection are already present, or if they develop in spite of the above procedures, the same treatment as for any case of acute iridocyclitis, including atropine, sulfanilamide, hot packs and further injections of foreign protein is indicated.

CONTUSIONS OF THE GLOBE.

After any sharp contusion of the globe *the pupil should be dilated* so that any signs of disturbance of the retina may be noted. The slightest edema of the retina, usually seen at the macular region, indicates the possibility that detachment of the retina may result, and this is especially the case if the eye is myopic. *Such eyes should be placed at rest for at least a week*, and the only method of securing such rest is the use of a bandage or shield over both eyes and strict confinement of the patient for that length of time, or longer, if the signs of retinal disturbance persist. After such signs have subsided the patient should be warned against stooping, straining or any strenuous exercise for a considerably longer time, as the appearance of retinal detachment may be delayed for weeks or months. The use of purges or sweats during the period of confinement has probably very little effect on the retinal edema, but the use of atropine is indicated in sufficient amounts to keep the pupil well dilated which indicates a corresponding relaxation of the ciliary muscle.

CONTUSIONS WITH INTRAOCULAR HEMORRHAGE.

The occurrence of slight hyphaema after a contusion is usually of no consequence, as the blood is absorbed within twenty-four to forty-eight hours without requiring any interference. Where the anterior chamber is completely filled with blood, however, *increased intraocular tension often develops.* The tension should be recorded in such cases, and if it is above

35 mm. (Schiotz) paracentesis is usually indicated. If the blood is still fluid enough it may be made to escape through the paracentesis wound by massage. Where it has coagulated firmly, and the tension is not reduced by paracentesis, it may be necessary to enlarge the opening and irrigate the anterior chamber. If the tension is not increased. even if the anterior chamber is full of blood, nothing need usually be done. The development of blood-staining of the cornea is rare in such cases, and the danger of its occurrence is not sufficiently great to warrant irrigation of the chamber in every case of hyphaema.

Little can be done for the complication of hemorrhage into the vitreous. If the amount of blood is not large it is usually absorbed slowly, while if the amount is large more or less dense opacities are apt to remain. It is questionable whether the administration of potassium iodide has any effect on the absorption of such blood, but it may be tried.

INTRAOCULAR FOREIGN BODY.

After any injury where the possibility of a retained intraocular foreign body exists roentgenograms should be made. If a foreign body exists it must be accurately localized with relation to the globe. While the Sweet localizer is very accurate, all ophthalmologists do not have this instrument at their disposal, nor a radiologist familiar with its use. Where this is the case the device used by H. Gifford of burying small pieces of silver wire beneath the conjunctiva to show the exact location of the globe on the roentgen-ray plate is exceedingly useful. After anesthetizing the conjunctiva by applications of 10 per cent cocaine a small vertical incision is made in the bulbar conjunctiva at the temporal side of the limbus above and below the cornea. This is undermined with a few snips of the scissors, and a piece of fine silver wire, 2 mm. long, is placed as near as possible to the limbus through each incision. Frontal and lateral roentgen-ray

plates are made, after which the wires are removed. No stitches are necessary. From these plates the location of the foreign body with relation to the cornea may easily be calculated. (See Figs. 68 and 69.) The bone-free method of Vogt consists in placing small books as markers in the conjunctiva, several exposures being made on dental roentgen-ray films which are pressed as far back into the orbit as possible on either side of the globe. This shows very small

Fig. 68.—Frontal roentgenogram showing silver-wire markers and foreign body just nasal to lower marker

foreign bodies, but only those which are in the anterior segment. With the information obtained by any of these localizing methods one may decide whether to attempt removal of the foreign body, which should always be done if it is in the globe and magnetic, or to leave it alone, which is usually safe when it has passed through the globe into the orbit.

After any such wound, with its possibilities of infection, atropine should be instilled, and a foreign protein injection given. Then full doses of sodium salicylate will usually be

advisable, to minimize the resulting iridocyclitis. When a non-magnetic foreign body is demonstrated in the eye it is seldom that it can be removed with safety, unless it is in the iris or lens. Such eyes should be kept under observation for a slow iridocyclitis which is often the prelude to sym-

FIG. 69—Lateral roentgenogram of same case, showing foreign body 7 mm. posterior to lower marker, hence inside the globe.

pathetic ophthalmia. While it would undoubtedly be safest to remove all eyes containing an unremovable foreign body, a number of such eyes have been saved with useful vision, and if vision is present the usual course is to watch the eye carefully and advise removal when definite symptoms of iridocyclitis persist.

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APPENDIX.

CONDITIONS, THE TREATMENT OF WHICH IS ON AN EXPERIMENTAL OR UNSATISFACTORY BASIS.

RETINITIS PIGMENTOSA.

This condition, and the closely related retinitis albescens punctata, have been the subjects of numerous reports during recent years, some of which have claimed a favorable influence on the disease by various methods of treatment. The cause of the disease is, of course, unknown, and evidence has seemed to indicate that the primary condition is a degeneration of the visual elements in the retina, these cells being replaced by proliferation of the pigment epithelium. The degeneration is perhaps always on an hereditary basis, but may be manifest in only one or a few members of a family. Since the cause could not be attacked, treatment has been directed at several of the symptoms and signs of the disease. One of the constant phenomena in retinitis pigmentosa is contraction of the retinal arteries. It was only natural, in view of recent results with sympathectomy for peripheral vascular spasm, that this procedure should be tried in retinitis pigmentosa with the idea of preventing further contraction of the vessels and hence stopping visual deterioration. Royle in 1930 and 1932 reported on 19 patients treated by *section of the sympathetic trunk* below the first thoracic ganglion and stated that in early cases, improvement in the visual fields resulted.

Meighen and Campbell have reported favorable results by removal of the superior cervical ganglion, and Magitot by stripping the carotid arteries of their peri-arterial sympathetic nerves. The reports of Meighen and Campbell were each based on one case, and that of Magitot on two cases of

retinitis pigmentosa, his method having been applied to cases of optic atrophy as well. MacDonald and Mackenzie in 1935 reported on four patients subjected to cervicothoracic sympathectomy, with slight improvement in the fields in two cases. They are very conservative in their judgment of the procedure and feel that long observation will be necessary for final judgment. Walsh and Sloan saw slight improvement in fields and adaptation in one out of three cases. de Takats and the author reported observations on six patients upon whom eleven operations were performed. In the first four operations, cervico-dorsal sympathectomy, and in the 7 others excision of the superior cervical ganglion was performed. The latter procedure was considered most logical, as it interrupts the sympathetic nerve supply more completely than lower sections. de Takats considered that Magitot's procedure of stripping the carotid arteries, which is even more complete in its effect, is not without danger of permanently elevating the blood-pressure. It was impossible to determine changes in the retinal circulation following either of the procedures employed in this series, though sympathetic denervation was indicated by the occurrence of a complete Horner's syndrome in most cases. *No definite improvement in fields or vision occurred in any case.* One patient showed further loss of field eight months after operation but in none of the others did any such deterioration occur. Thus the impression obtained from this series was not in agreement with the reports of Royle. If it were possible to state that progress of the disease is slowed or halted by this procedure it would be well worth while. It is too soon for even this statement to be made however, since progress of the disease is known to be exceedingly slow in many cases. No serious ill effects of the operation itself have been reported, nor were any observed in this series. *If the procedure is employed, it should be used in early cases, and the patient should be made to understand that the results are as yet uncertain.* Careful records of adaptation as well as of fields and vision

should be made before and frequently after operation, so that more definite evidence concerning the results will be available.

The predominance of pigment in the fundus picture led Luedde to treat the condition with injections of an *antigen made from uveal pigment*. Results were not convincing, however, and no later report has appeared. This is what might be expected on the now generally accepted theory that the pigment changes form a purely secondary phenomenon in the disease. This also makes it difficult to believe in a theory recently proposed that a derangement in pituitary secretion because of the relation of the gland to melanogenesis may be a factor in retinitis pigmentosa.

The use of *female gonadal extracts* by Wibaut rests upon a somewhat fanciful hypothesis. Wibaut believed that because of the slightly greater incidence of the disease in men as compared with that in women (about 55 to 45 per cent), some substance might be present in the blood of women which prevented the appearance of the degenerative phenomena. He employed "*Menformon*," a substance prepared from the urine of pregnant women, and reported improvement in patients so treated. He employed 100 mouse units subcutaneously or 250 to 500 by mouth daily. Out of 31 cases treated improvement was marked in 1, definite in 7 and doubtful or absent in the remainder. None of the cases in his early reports seemed to have been followed longer than two or three months. Kestenbaum reported a case treated with an ovarian extract and large amounts of liver in which definite enlargement of the fields occurred and was maintained during several years' observation. Bunge saw moderate improvement in 2 of 5 cases treated. Meller and Sallmann, however, tried the method in a number of cases without success. In considering these reports, the suggestibility of patients with this disease, and the possibility that the mental effect of a new treatment caused certain patients to report better fields and vision must be considered. In the

face of a theoretical basis so unsatisfactory and reported results so at variance, *skepticism with regard to this method seems justified* until a much greater body of clinical evidence appears than is at present available. It might be justified, in women with other symptoms of glandular deficiency to supply a potent ovarian extract.

In view of the relation of hemeralopia to *vitamin A deficiency* it was natural that attempts should be made to influence this symptom in retinitis pigmentosa by supplying this vitamin. The effect of liver on night-blindness had long been known and the ingestion of large amounts of liver was first tried in retinitis pigmentosa. Levine reviewed the theoretical reasons for considering a relationship between vitamin A deficiency and retinitis pigmentosa. He used large doses of cod-liver oil in a series of cases and although temporary improvements in vision were noted in some patients, they were not permanent. Casini reported some increase of field in one case. The author has tried *the combined effect of vitamin A concentrates and a vasodilator* (sodium nitrite, three grains a day), and was surprised to see a marked improvement of fields and central vision in one case and a moderate improvement in a second. In the first case this improvement has been maintained for only three months, while in the second case the fields during the course of a year have returned to about the size present before treatment was begun. In a third case some improvement in central vision was recorded, but none in the fields, while in a fourth case the fields became somewhat worse during treatment. It is impossible to draw conclusions from such a small number of cases, and it is to be feared that the ultimate results of this method, like those of others proposed for this disease, will prove to be a disappointment. In such a condition, however, attempts to confirm the results of others obtained on a purely empirical basis would seem justified, provided the patient is not subjected to procedures involving danger or needless expense.

close work seems unnecessary to the author, though moderation will be advised by those who believe the influence of close work is a factor in myopia. It seems to the author unwise ever to advise taking a child out of school because of progressive myopia. Bodily exercise should be encouraged and a well-balanced diet containing the necessary amount of vitamins should be maintained. Advice on the proper posture for reading should be given. A general physical examination may be wise where myopia is rapidly increasing, as it is possible that improvement in general health may be of value in halting the process.

Epinephrin was employed by Wiener because of the effect he observed on ectatic corneal scars. He believed the shrinking effect produced on such tissues by epinephrin might influence the ocular tissues, and imagined that a deficiency of adrenal secretion might be present in patients with progressive myopia. He reported on a number of patients in whom myopia became stationary during its use. He employed 1 to 1000 epinephrin by instillation several times a day for long periods. Others have employed the method, but no accurate statistics have been published aside from those of Wiener. It is difficult to conceive of any mechanism by which the absorption of epinephrin given in this way could have any effect on the progress of myopia, and the apparent result in any case seems most easily explained as a spontaneous phenomenon coincident with the beginning of treatment.

Bothman reported on the frequency with which evidences of *thyroid insufficiency* as shown by a low basal metabolism is observed in progressive myopia. The abnormalities in metabolism noted were in most cases slight and tests were seldom repeated. The evidence was not sufficient, in the author's opinion, to justify the use of thyroid extract which was recommended in these cases. Where signs of glandular imbalance are present, such as obesity or abnormal growth

phenomena, an examination of the endocrine system is indicated, but *it has not yet been shown that glandular therapy is of value in progressive myopia.*

The same may be said of the use of viosterol which has recently been advocated by Arthur Knapp. An adequate supply of this vitamin is certainly necessary to normal nutrition, but the author cannot agree that the requirements of myopes are any greater than those of normal individuals.

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